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EXPERIMENTAL FRICTION BLISTERS.

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FRICTION applied to skin may cause either of two main types of reaction.

Firstly, if the friction is small in amount but frequently repeated the skin may react by becoming thicker. This occurs over a period of weeks or months and may be regarded as a chronic frictional reaction. Chronic frictional reactions may appear in several distinct clinical forms and the factors which govern the type of reaction remain obscure. This is a result of the practical difficulties involved in conducting such necessarily prolonged and carefully controlled experiments.

Secondly, larger amounts of friction may cause the skin to react by the formation of a blister. This may occur during a period of minutes and may be regarded as an acute frictional reaction. The study of acute frictional reactions, which appear in several minutes, presents fewer practical difficulties. The quantitative aspects and pathogenesis of friction blisters have been investigated.

PART I.

The Production of Experimental Friction Blisters and the Measurement of the Stimulus Required for their Production.

Naturally occurring friction blisters are usually formed in sites where the stratum corneum is thick, as on the soles and palms. The thick stratum corneum causes a delay between the time of blister formation and the blister becoming clinically apparent. The thin stratum corneum over the anterior surface of the tibia ensures that blisters rupture as soon as they are formed. This rupture, which occurs very suddenly during the course of one rub, is a convenient endpoint for an all-or-none response to the friction.

Method.

The technique consists of rubbing an area of skin over the middle third of the anterior surface of the tibia at a constant speed and loading weight until a blister forms and ruptures. The rubbing is performed mechanically with the machine and by the method previously described (Naylor, 1955) and the frictional force between the skin and polythene friction head is recorded continuously.

During the rubbing the skin becomes red and slight flaking of the stratum corneum occurs. Suddenly the epidermis ruptures, producing a shallow crater

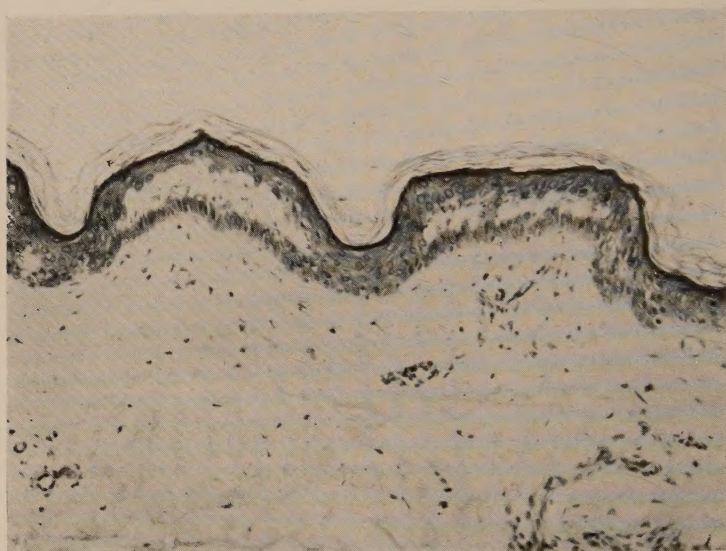


FIG. 1.—An experimental friction blister approximately 2 hours after rubbing.
H. & E. $\times 140$.

with sharp edges and a moist base. At the same moment a sudden pain is felt. The area of the crater may be extended by picking up its edges with forceps when a layer of cleavage in the epidermis extending beyond the margin of the original crater may be demonstrated.

If the rubbing is stopped just before epidermal rupture, a small flaccid blister may develop.

Results.

Histologically all the experimental friction blisters appear to be identical (Fig. 1). The essential changes are a necrosis of the prickly cells and the formation of small intra-epidermal vesicles which coalesce to form larger vesicles. There is no acantholysis. In the dermis there is some oedema and if the biopsy

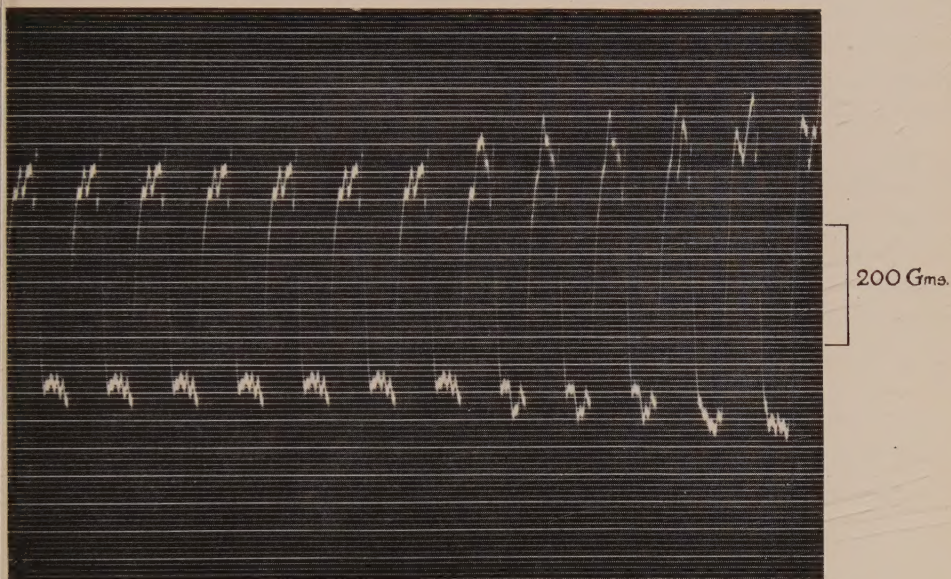


FIG. 2.—Recording of the frictional force between skin and polythene at the moment of epidermal rupture. Rubbing speed 1 cycle in 3 seconds. Vertical load 530 g.

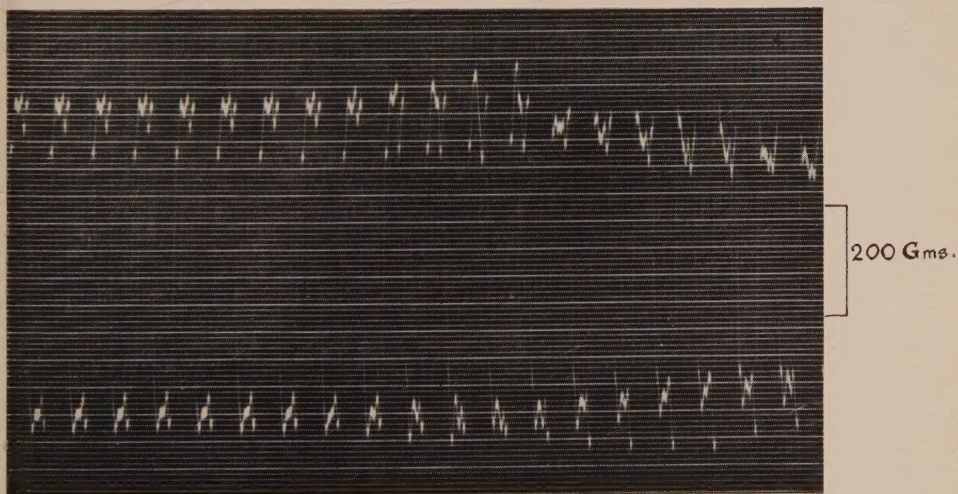


FIG. 3.—Recording of the frictional force between skin and polythene at the moment of epidermal rupture showing an initial rise in the frictional force followed by a fall. Rubbing speed 1 cycle in 3 seconds. Vertical load 530 g.

is performed immediately the oedema fluid is confined to the areas around the blood vessels. There is no spongiosis.

The roofs of recent naturally occurring friction blisters have been examined histologically. They all consist of partial epidermal thickness and show prickle-cell necrosis.

The sudden rupture of the epidermis is shown in the recording of the frictional force between the skin and friction head by a change in the previously regular pattern of friction (Fig. 2). A similar record shown in Fig. 3 illustrates the effect of moisture at the moment of blistering. Initially, there is a small leak of blister fluid which spreads on to the surrounding skin and causes a rise in the frictional force. This sudden rise causes the remainder of the surface to rupture with more release of fluid and the frictional force falls again.

During most experiments there is a gradual increase of the frictional force between the skin and polythene friction head. The increase is usually small and always bears a linear relationship to the number of rubs administered. An average of the frictional force at the beginning of the experiment and the frictional force immediately before epidermal rupture is calculated from the recording and is taken as the relevant frictional force in each experiment. This figure, together with the number of rubs, measures the stimulus required for production of the blister.

DISCUSSION.

Lesions comparable with these experimental blisters which occur in sites where the skin has a thin stratum corneum are familiar to all amateur gardeners. They usually occur on the sides of the fingers during the vigorous use of a hoe or rake. The first indication of any lesion is sudden pain; a raw area on the side of a finger appears simultaneously. The roof of the blister is usually left attached to one side of the lesion. The process is painless until the sudden rupture of the epidermis.

PART II.

The Effect of Skin Surface Conditions upon the Stimulus Required for the Production of Friction Blisters.

The susceptibility of the skin to frictional trauma has often been observed clinically to depend upon environmental conditions and in particular upon the presence of sweat and moisture. Whitfield (1932) observed that the damp extremity has a greater tendency to blister and the dry extremity a greater tendency to the formation of callosities. Roxburgh (1950) states that prolonged wetness of the skin causes maceration of the horny layer, which then ceases to form an efficient protective covering and renders the skin more liable to injury. Schwartz, Tulipan and Peck (1947) hold a similar view. Loewenthal

(1950) states that prolonged sweating causes the sweat to become more alkaline and this increases the maceration of the stratum corneum.

Grease and moisture can cause the coefficient of friction between skin and polythene to vary by 100 % and therefore the frictional force resulting from a constant loading weight can vary by this amount (Naylor, 1955). The effect of these skin surface frictional phenomena upon the susceptibility of skin to blister formation has been measured.

Method.

The technique is that of rubbing areas of skin over the middle third of the anterior surface of the tibia at a constant speed and loading weight, and recording continuously the frictional force between the skin and rubbing agent until a blister forms and ruptures as described in Part I, above.

The subjects were nineteen male medical students and doctors, aged eighteen to thirty-three years. One blister was produced on each leg on two occasions, making a total of four blisters on each subject. On the first occasion, the most inferior position on one side and the most superior position on the contralateral side were chosen for rubbing. The positions were reversed on the two sides on the second occasion. This procedure was followed to randomize any possible effect which the position might have on the results.

The skin in these experiments was prepared only by removing the long hairs with scissors; variations in skin surface conditions were provided by accepting, without skin preparation, each subject as he presented. Wet and dry bulb thermometer readings were taken and recorded on each occasion.

In addition to the nineteen students, blisters were produced on a further eleven normal male volunteers of the same age group, whose skin was prepared by blowing a puff of powdered talc on the skin at the beginning of each experiment to lower the frictional force. Four of the eleven volunteers were subjected to two experiments on one occasion, and the remaining seven were subjected to single experiments.

In all experiments the friction head was made of polythene, the speed of rubbing 1 cycle in 3 seconds, and the loading weight 530 g.

Results.

The results, expressed in terms of the two variables, number of rubs required to produce a blister and frictional force at a load of 530 g., are shown in Table I.

The frictional force resulting from a load of 530 g. and the number of rubs required to produce a blister were averaged for the two sides for each subject on each occasion, and are shown in the form of a graph (Fig. 4). The graph also includes the results from the eleven volunteers whose skin was prepared with powdered talc before each experiment.

TABLE I.—Results of All Blistering Experiments showing the Recorded Frictional Force and Number of Rubs to Blister Formation. Constant vertical load of 530 g.

Normal subjects: skin unprepared.

Subject.	Occasion 1.		Occasion 2.		Occasion 3.	
	WB = 9.	DB = 17	WB = 13.	DB = 19	WB = 11.7.	DB = 20.4
(1) W. O. M—	LS: F = 277. N = 51	RI: F = 246. N = 75	LI: F = 282. N = 45	RS: F = 252. N = 62	LM: F = 224. N = 55	RM: F = 247. N = 55
(2) J. M. D. G. P—	WB = 14.8.	DB = 22	WB = 9.5.	DB = 15	WB = 13.	DB = 20.5
	LI: F = 224. N = 75	RI: F = 236. N = 68	LS: F = 294. N = 42	RS: F = 282. N = 28	LM: F = 227. N = 90	RM: F = 204. N = 130
(3) R. W. W. K—	WB = 15.	DB = 23	WB = 13.	DB = 20.5	WB = 15.	DB = 23.5
	LS: F = 265. N = 67	RI: F = 243. N = 88	LI: F = 304. N = 51	RS: F = 285. N = 53	LM: F = 315. N = 41	RM: F = 330. N = 31
(4) B. J. G. S—	WB = 14.	DB = 22	WB = 15.	DB = 21	WB = 14.7.	DB = 19
	LS: F = 276. N = 41	RI: F = 266. N = 44	LI: F = 285. N = 29	RS: F = 288. N = 32	LM: F = 280. N = 47	RM: F = 268. N = 50
(5) M. H. K—	WB = 13.5.	DB = 21	WB = 12.	DB = 21	WB = 13.5.	DB = 22
	LS: F = 267. N = 37	RI: F = 275. N = 22	LI: F = 312. N = 30	RS: F = 304. N = 30	LM: F = 328. N = 36	RM: F = 325. N = 20
(6) J. E. W. W—	WB = 13.5.	DB = 21.5	WB = 15.	DB = 21.5	WB = 15.5.	DB = 19.3
	LS: F = 270. N = 59	RI: F = 262. N = 98	LI: F = 286. N = 65	RS: F = 283. N = 54	LM: F = 273. N = 70	RM: F = 286. N = 50
(7) C. D. E—	WB = 14.	DB = 22	WB = 11.3.	DB = 20.3	WB = 17.2.	DB = 21.5
	LS: F = 295. N = 30	RI: F = 292. N = 34	LI: F = 299. N = 46	RS: F = 279. N = 42	LM: F = 308. N = 33	RM: F = 300. N = 40
(8) A. J. P—	WB = 12.5.	DB = 20	WB = 14.8.	DB = 22.5	WB = 14.3.	DB = 18
	LS: F = 269. N = 61	RI: F = 287. N = 42	LI: F = 278. N = 64	RS: F = 294. N = 59	LM: F = 263. N = 90	RM: F = 239. N = 62
(9) H. W. H—	WB = 13.	DB = 21.5	WB = 13.3.	DB = 20.5	WB = 15.7.	DB = 19.5
	LS: F = 265. N = 40	RI: F = 265. N = 40	LI: F = 264. N = 48	RS: F = 280. N = 32	LM: F = 282. N = 40	RM: F = 319. N = 27
(10) P. H—	WB = 12.3.	DB = 20	WB = 11.7.	DB = 20.7	—	—
	LS: F = 281. N = 47	RI: F = 260. N = 38	LI: F = 251. N = 36	RS: F = 248. N = 49	WB = 13.5.	DB = 20
(11) M. J. M—	WB = 14.3.	DB = 22.8	WB = 14.	DB = 22	WB = 13.5.	DB = 20
	LS: F = 249. N = 78	RI: F = 233. N = 68	LI: F = 273. N = 64	RS: F = 253. N = 48	LM: F = 256. N = 33	RM: F = 249. N = 50
(12) M. A. E. S—	WB = 13.	DB = 22	WB = 15.	DB = 20	WB = 10.	DB = 14
	LS: F = 244. N = 53	RI: F = 252. N = 35	LI: F = 285. N = 28	RS: F = 263. N = 60	LM: F = 250. N = 72	RM: F = 251. N = 75
(13) M. H. M—	WB = 12.	DB = 21.5	WB = 14.8.	DB = 21.3	WB = 15.	DB = 20
	LS: F = 254. N = 66	RI: F = 281. N = 64	LI: F = 349. N = 32	RS: F = 348. N = 34	LM: F = 267. N = 49	RM: F = 272. N = 40
(14) J. R—	WB = 12.5.	DB = 21.5	WB = 14.8.	DB = 21	—	—
	LS: F = 244. N = 36	RI: F = 237. N = 31	LI: F = 233. N = 118	RS: F = 266. N = 60	WB = 14.5.	DB = 18.5
(15) P. M. T. M—	WB = 11.	DB = 19	WB = 14.	DB = 21.5	WB = 14.5.	DB = 18.5
	LS: F = 240. N = 71	RI: F = 233. N = 71	LI: F = 221. N = 92	RS: F = 270. N = 79	LM: F = 264. N = 81	RM: F = 252. N = 85
(16) E. S. G—	WB = 11.	DB = 18	WB = 15.	DB = 23.5	WB = 15.	DB = 19.5
	LS: F = 291. N = 64	RI: F = 249. N = 62	LI: F = 256. N = 50	RS: F = 252. N = 49	LM: F = 262. N = 51	RM: F = 283. N = 61
(17) J. V—	WB = 11.5.	DB = 19.5	WB = 13.7.	DB = 19.5	WB = 13.4.	DB = 19.3
	LS: F = 334. N = 33	RI: F = 278. N = 52	LI: F = 312. N = 32	RS: F = 300. N = 30	LM: F = 281. N = 50	RM: F = 316. N = 24
(18) J. W—	WB = 12.	DB = 20	WB = 14.5.	DB = 22.5	WB = 13.5.	DB = 21.5
	LS: F = 305. N = 36	RI: F = 261. N = 46	LI: F = 348. N = 30	RS: F = 310. N = 40	LM: F = 306. N = 40	RM: F = 258. N = 44
(19) B. K—	WB = 13.8.	DB = 18.8	WB = 12.	DB = 18.8	WB = 16.5.	DB = 23.5
	LS: F = 339. N = 26	RI: F = 307. N = 27	LI: F = 284. N = 25	RS: F = 283. N = 37	LM: F = 266. N = 25	RM: F = 274. N = 32

Occasions 1 and 2: Polythene friction head. Rubbing speed: 1 cycle in 3 seconds.

Code: R = right; L = left; S = superior; M = middle; I = inferior; WB = wet bulb temperature (°C); DB = dry bulb temperature (°C); F = frictional force, g.; N = number of rubs to blister formation.

TABLE I (*continued*).*Normal subjects: skin prepared with talc.*

Subject.	Occasion 1.
(1) B— .	WB = 10·7. DB = 17·7 LM : F = 225. N = 115 RM : F = 234. N = 104
(2) M— .	WB = 13. DB = 19·5 LM : F = 201. N = 83 RM : F = 187. N = 92
(3) P.H— .	WB = 9·5. DB = 19·5 LM : F = 211. N = 84 RM : F = 199. N = 97
(4) D. N. H— .	WB = 17·5. DB = 22 RM : F = 274. N = 44 LM : F = 271. N = 41
(5) P— .	WB = 11·2. DB = 19 LM : F = 228. N = 123
(6) J. B— .	WB = 12. DB = 17·5 LM : F = 220. N = 120
(7) W. D. F— .	WB = 12·3. DB = 18·8 LM : F = 224. N = 138
(8) B. C— .	WB = 12·5. DB = 18·5 LM : F = 229. N = 121.
(9) R. D. B— .	WB = 10. DB = 16 LM : F = 219. N = 94
(10) I. M— .	WB = 10. DB = 16 LM : F = 227. N = 123
(11) C. D. E— .	WB = 11·3. DB = 20·3 LM : F = 243. N = 95

Dermographia patients: skin unprepared.

Subject.	Occasion 1.
(1) M. B. M— .	WB = 12·8. DB = 20·8 LM : F = 282. N = 32 RM : F = 239. N = 74
(2) H. B. C— .	WB = 11. DB = 20·5 LM : F = 276. N = 35 RM : F = 282. N = 27
(3) D. R— .	WB = 14·7. DB = 20 LM : F = 303. N = 30 RM : F = 254. N = 92

Chronic urticaria patients: skin unprepared.

Subject.	Occasion 1.
(1) S— .	WB = 15·2. DB = 23·8 LM : F = 267. N = 44 RM : F = 277. N = 49
(2) H. M. T— .	WB = 13·5. DB = 19 LM : F = 355. N = 36 RM : F = 277. N = 35
(3) S. S— .	WB = 11·5. DB = 18·5 LM : F = 325. N = 32 RM : F = 285. N = 33

The average frictional force varied between 194 and 348 g. The average number of rubs required to produce a blister varied between 138 and 27. There is an inverse relationship between the two variables.

Statistical analysis of the results from the nineteen students and doctors was performed separately for the right and left legs.

There is an inverse relationship between the frictional force and the number of rubs required to produce a blister. Although there is a total variation, there is no evidence that, for the same subject, the number of rubs required to produce a blister varies from one occasion to another if variations in the frictional force

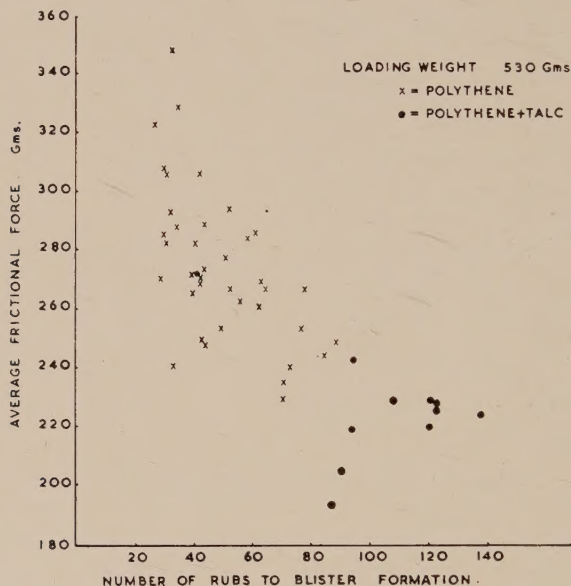


FIG. 4.—The effect of the frictional force on the number of rubs to blister formation.

receive due allowance. There is no evidence that, for different normal subjects the number of rubs required to produce a blister varies, again if variations in the frictional force receive due allowance.

DISCUSSION.

It has been shown (Naylor, 1955) that the surface conditions of skin control the coefficient of friction between skin and polythene. The experiments described above show that the coefficient of friction between skin and the rubbing agent affects the number of rubs which the epidermis can withstand before it ruptures. Factors which increase the coefficient of friction, such as moisture, reduce the number of rubs which the skin can withstand. Factors which

increase the coefficient of friction, such as grease and powdered talc, increase the number of rubs which the skin can withstand.

It can be seen from Table I that in these experiments there is no obvious correlation between wet and dry bulb thermometer readings and the recorded frictional force, in spite of the known effect of environmental conditions upon the coefficient of friction between skin and polythene. This lack of correlation is probably due to the presence of so many other possible variables, such as individual variations of sweating under similar environmental conditions,

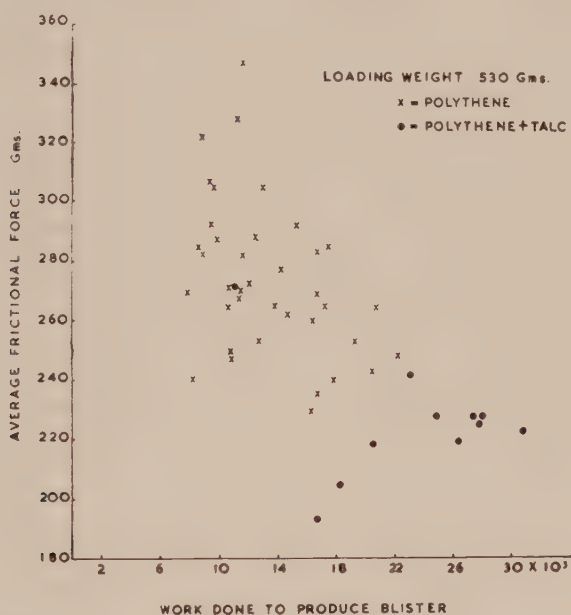


FIG. 5.—The effect of the frictional force on the work done to produce a blister.

the time since each subject bathed and the amount of exercise which each subject had taken immediately before the experiment.

It might be supposed, from general principles, that the product of the average frictional force and the average number of rubs required to produce a blister could be a constant, proportional to the amount of work needed to produce a blister. Fig. 5, which is a graph obtained by plotting this product against the average frictional force, does not support this view. It appears from this graph that the lower the frictional force the greater the amount of work the epidermis can withstand before rupture. This may represent a degree of recovery by the epidermis occasioned by the longer time which passes before epidermal rupture. The results from experiments in which the rubbing speed was increased, to be described in Part III, do not support this view. Alternatively, the same

surface conditions as are responsible for an alteration in the frictional force may also cause a change in the physical properties of the keratin layer covering the vesicles and change the ease with which they rupture. This alternative would be consistent with the views of Roxburgh (1950) and of Schwartz and his co-workers (1947). Yet another possible explanation is that it may represent a shift in the position of the endpoint of epidermal rupture. This possibility will now be considered.

It appears from the histological studies that the superficial layers of the epidermis are pulled back when small fluid vesicles have formed in the prickle cell layer, or when these small vesicles have coalesced to form a larger vesicle of critical size. If this hypothesis is correct the frictional force applied to the skin governs not only the amount of work done on the skin per rub, but in addition governs the degree of epidermal damage which is required before the endpoint is reached.

Consider two experiments, the first in which the frictional force is F and the second in which it is $\frac{F}{2}$. In the first experiment the epidermis ruptures after n rubs and the amount of work done to produce a blister is proportional to Fn . In the second experiment, to do the same amount of work on the skin will require $2n$ rubs. After n rubs in the first experiment and $2n$ rubs in the second experiment, the amount of work done on the skin, the degree of epidermal damage and the size of the intra-epidermal vesicles will be the same. At this point, in the first experiment F is large enough to rupture the vesicles and the epidermis will be pulled back. In the second experiment $\frac{F}{2}$ is not large enough to rupture the identical-sized vesicles and the epidermis will not be pulled back; additional damage will have to be done to the epidermis to increase the size of the vesicles until they are sufficiently large to be ruptured by $\frac{F}{2}$. An increase in the amount of work needed to reach the endpoint is thereby produced. This possibility has been considered previously (Naylor, 1952), but was then based only on theoretical considerations.

Whatever the mechanism involved, it appears that a lowering of the frictional force acting upon the skin affords protection in two ways: firstly, by lowering the amount of work done upon the skin per rub; secondly, by increasing the total work which the epidermis can withstand before rupture.

The observation, made by Whitfield (1932), that friction tends to produce blisters on damp skin and callosities on dry skin, may be explained by the reduction of the frictional force when the skin is dry. A stimulus which would provoke an acute frictional reaction when applied to moist skin is modified and provokes a chronic frictional reaction when applied to dry skin.

The practical application of these findings is well known, and it is common practice for soldiers to cover their feet with either talcum powder or hair-oil before a route march.

PART III.

The Pathogenesis of Friction Blisters.

Modern views on the mechanism of friction accord well with the classical concepts (Bowden and Tabor, 1950). Studies with the electron microscope and by oblique sectioning reveal that the most carefully prepared and polished surfaces contain irregularities which are very large in comparison with molecular dimensions. These surface irregularities are so large that the actual area of contact between surfaces is extremely small and bears very little relationship to the apparent area of contact. As the actual area of contact is so small the pressure developed at the summits of the irregularities is very high and plastic deformation and flow occur at these points until the actual area of contact is sufficiently large to support the load. It is thought that friction occurs only over the actual area of contact, and as this is proportional to the load and is independent of the apparent area of contact, the two fundamental laws of friction are satisfactorily explained.

When there is relative movement between two surfaces the friction occurring at these small points of contact produces localized areas of very high temperature at even moderate speeds of movement. The actual temperatures reached in these small areas will depend, among other things, upon the thermal conductivity of the two materials in contact. It is thought that the surface temperature should vary inversely as the square root of the thermal conductivity; thus, if the materials are poor conductors of heat, the temperatures produced may be extremely high. The intense heating, which is confined to a thin layer in the region of the actual contact, occurs in the absence of any obvious temperature change of the material as a whole.

Study of the damage caused by friction between non-biological materials shows that this damage is confined to the surface layers and the layers close to the surface, and is largely caused by the shearing and plucking out of the minute junctions formed under the intense pressure.

The problem of frictional damage to skin is very different. Although friction must produce alteration and damage of the surface layer of squames or dead epithelial cells, it produces more important changes in the living epithelial cells, which are more deeply situated, and possibly also in the cells of the dermis.

In spite of this fundamental difference, it has been shown in Part II that knowledge of the physical conditions at the skin surface, and in particular the degree of lubrication, appears to be important. Detailed study of these surface phenomena is hampered by inability to standardize conditions at the skin surface and by difficulty in applying the techniques used in experiments upon non-biological material.

The essential histological changes in the production of friction blisters are prickle-cell necrosis and the formation of small intra-epidermal vesicles. The

cause of the prickle-cell necrosis and the origin of the fluid in the vesicles is uncertain. Experiments have been performed which help to clarify these problems.

Method.

Seventeen of the nineteen subjects who were studied in Part II had one more blister produced on each leg. The position chosen for rubbing was an area of skin between the two sites which were blistered on occasions (1) and (2) as described in Part II. The seventeen subjects were divided into four groups and in each group one of the experimental conditions which was constant on occasions (1) and (2) was altered for this their last attendance, on occasion (3). The changed conditions in each group were as follows :

(i) A silver friction head of identical size and shape was used in place of polythene. The speed of rubbing was 1 cycle in 3 seconds and the loading weight 530 g., as in the main series.

(ii) The speed of rubbing was increased to 1 cycle in 2 seconds. The polythene friction head was used at a loading weight of 530 g.

(iii) An arterial cuff was placed round the thigh and rapidly inflated to 200 mm. Hg. from an air reservoir immediately before starting the experiment. The cuff was maintained at this pressure until the blister had formed and burst. The polythene friction head was used at a speed of 1 cycle in 3 seconds at a loading weight of 530 g.

(iv) A reactive hyperaemia was induced by an arterial cuff, employed as in Group (iii). The cuff was maintained at 200 mm. Hg for ten minutes and was released immediately before the rubbing started. This produced a reactive hyperaemia for 4-5 minutes as judged by the colour and temperature of the skin. The polythene friction head was used at a speed of 1 cycle in 3 seconds at a loading weight of 530 g.

In addition to the above groups, experimental blisters were produced on three dermatographia patients and three patients with chronic urticaria, using the polythene friction head at a speed of 1 cycle in 3 seconds and a loading weight of 530 g.

A single experiment was performed on a piece of skin removed from a patient during an operation for radical mastectomy. The fat was dissected away and the skin pinned to a cork board. An experimental friction blister was produced within 20 minutes of the blood supply having been severed. The blistered area was then sectioned.

Results.

The results of these experiments are shown in Table I. The results from the two sides have been averaged for each subject for his third attendance,

and have been presented by superimposing the points so derived upon the points obtained in the same way on occasions (1) and (2), and already shown in Fig. 4. This has been done separately for each of the four groups and is shown in Figs. 6, 7, 8 and 9. This procedure enables the effect of changing one variable to be seen against a background of controls.

The results from the nineteen normal subjects which were presented in Part I and shown graphically in Fig. 4 show no difference in the number of rubs needed to produce a blister between occasions or between subjects, if differences in the frictional force receive due allowance. The method of presentation of the results which has been adopted above would therefore seem justifiable.

No difference was detectable between the effect of the silver and polythene friction heads at comparable frictional forces (Fig. 6).

The increased speed of rubbing produced no measurable difference in its effect from the slower speed (Fig. 7).

Ischaemia and reactive hyperaemia produced no measurable differences in the susceptibility of the skin to blister formation (Figs. 8 and 9).

The results from the dermatographia patients and the patients with chronic urticaria are shown in Table I, and have also been presented graphically in the same way as the four groups of normal subjects (Fig. 10). These patients were not ideal for experimental purposes in that four of them (D. R—, S—, H. M. T— and S. S—) were females, and of the remaining two males, one (H. B. C—) was aged 49 years. The thirty controls were all males aged 18–33 years. With these reservations, all behaved as normal subjects.

The experimental data from the four groups of normal subjects on their first attendance and from the dermatographia and chronic urticaria patients have not been subjected to statistical analysis because, as can be seen from Figs. 6, 7, 8, 9 and 10, their points on these graphs lie within the scatter of results from the experimental data obtained from the thirty normal subjects.

Histological examination of the skin which was blistered after its removal from the patient showed prickle-cell necrosis and the presence of small intra-epidermal vesicles.

DISCUSSION.

The primary histological changes in the production of experimental friction blisters are necrosis of the prickle cells and the formation of small intra-epidermal vesicles. Necrosis of the prickle cells may be due to direct physical damage caused by the friction, or the friction may initiate some enzymic process which causes the damage. Direct physical damage to the cells may be due either to local heating effect or to repeated mechanical distortion of the cells.

If a rise in temperature at the skin surface were responsible for the damage to the prickle cells, a silver friction head which has a high thermal conductivity would afford protection to the skin compared with polythene, which has a low

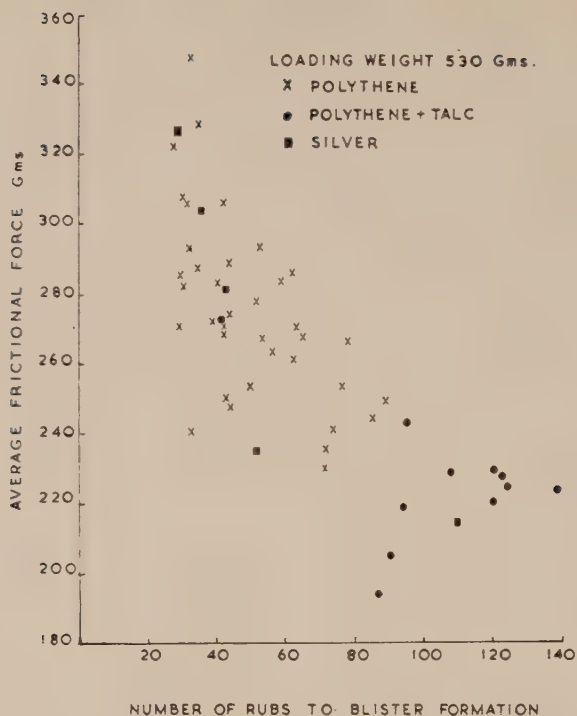


Fig. 6.—A comparison of polythene and silver in the production of experimental friction blisters.

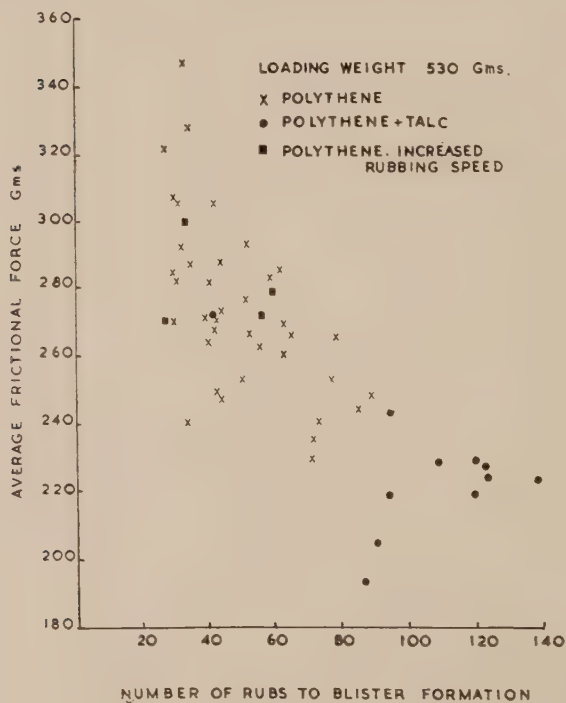


Fig. 7.—The effect of rubbing speed on the production of experimental friction blisters.

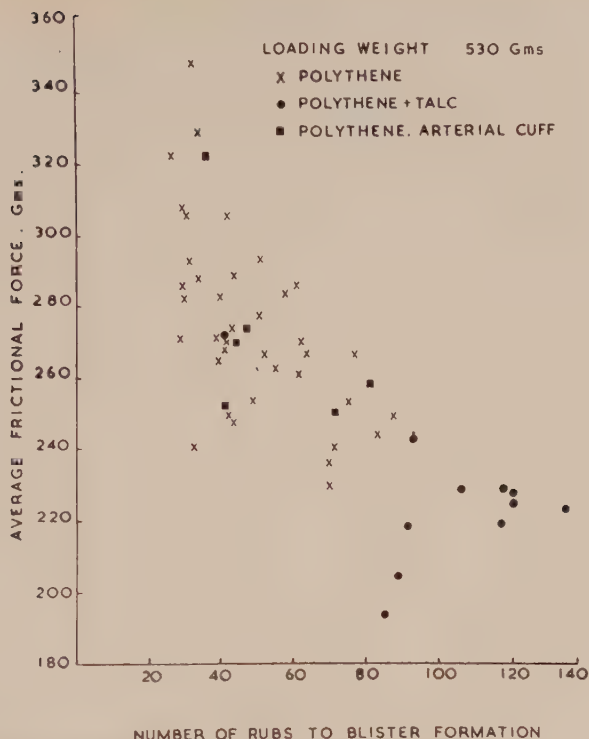


FIG. 8.—The effect of skin ischaemia on the production of experimental friction blisters.

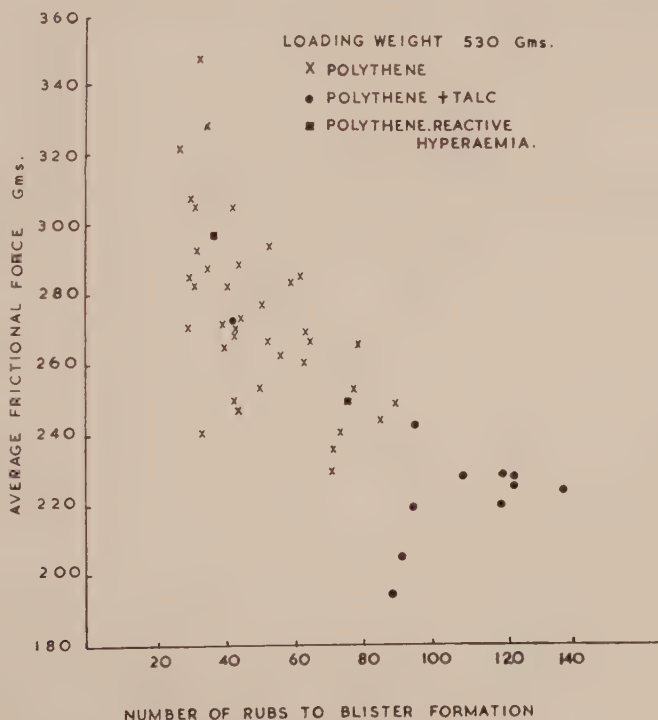


FIG. 9.—The effect of skin reactive hyperaemia on the production of experimental friction blisters.

thermal conductivity. The results shown in Fig. 6 show that at comparable frictional forces, silver and polythene are equally damaging.

Rubbing the skin at an increased speed should produce higher local rises in temperature by producing more heat and allowing less time for its dissipation between successive rubs. The results in Fig. 7 show that a 50% increase in the speed of the friction head produces no increase of epidermal damage at comparable frictional forces.

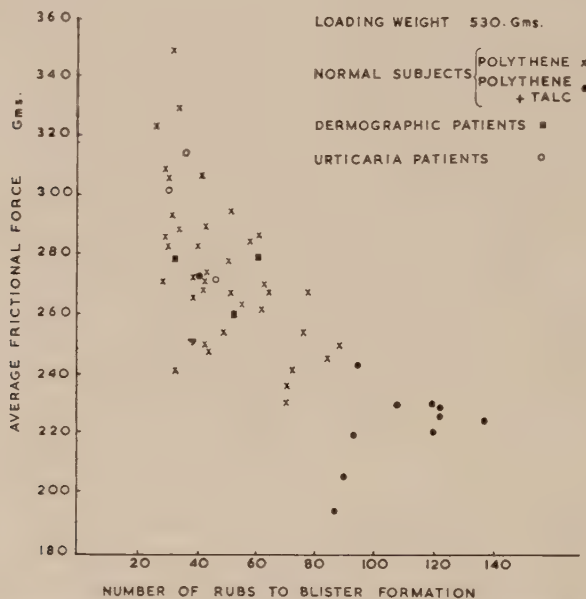


FIG. 10.—A comparison between normal subjects, urticaria patients and dermatographia patients in their susceptibility to experimental blister formation.

Although no attempt has been made to measure directly any rise of temperature at the skin surface caused by the friction, these two series of experiments make local rise of temperature, as a cause of prickle-cell necrosis, appear unlikely.

The histological changes resulting from friction cannot be attributed to a histamine effect, as the dermatographia patients and patients with chronic urticaria do not show any increased susceptibility to friction.

The distribution of the points in Fig. 4 shows that, at the higher frictional forces, a large increase in the frictional force produces only a small reduction in the number of rubs required to produce a blister. In no experiment was the average number of rubs below 27. The time taken to complete 27 rubs is 81 seconds and, alternatively, it may be said that the time taken to produce a blister could not be reduced below 81 seconds. It is possible that this time

represents either the minimum time necessary to complete an enzymic reaction or the minimum time necessary for fluid to reach the epidermis from the dermis and form the intra-epidermal vesicles. If there were a minimum time limit of approximately 81 seconds an increased speed of rubbing would enable more rubs to be given during this time and an apparently increased tolerance to friction would be shown. The points in Fig. 7 obtained by rubbing at a 50% increased speed show no detectable difference from the slower speed. This makes the hypothesis unlikely and suggests that the limiting factor is not time, but rather the number of rubs administered.

Experiments performed during extreme acute alterations in blood flow, produced by arterial occlusion and reactive hyperaemia, show no detectable difference in their results from the experiments with average blood flow, and a blister produced in skin completely severed from its blood supply has the same histological appearance as a blister produced in skin with an intact blood supply. It therefore appears unlikely that dermal fluid is responsible for the intra-epidermal vesicles. This view is supported by the absence of spongiosis and by the fact that dermal oedema is confined to the perivascular areas if the biopsies are performed immediately.

Naturally occurring friction blisters often contain a large volume of fluid and it seems that this fluid must originate from the dermis.

Blister formation may, therefore, be regarded as occurring in two independent stages: first, the formation of an intra-epidermal split by prickle-cell necrosis, and, second, the distension of this split with fluid, presumably from the dermis. It is the ease with which the intra-epidermal split is produced which is being measured in these experiments.

The mechanism of the prickle-cell necrosis which is responsible for the intra-epidermal split remains unexplained, but a hypothesis which agrees with all the observations is that it is due to repeated distortion of the prickle cells; this might cause a denaturation of the cellular protein.

SUMMARY.

A technique has been developed for producing experimental friction blisters and for measuring the stimulus required for their production. All experiments have been performed on skin overlying the middle third of the anterior surface of the tibia using polythene or silver as the rubbing agent.

Variations in the coefficient of friction between skin and the rubbing agent make it impossible to define frictional trauma in terms of the two variables, number of rubs and vertical load. The frictional force between the two surfaces must be recorded.

The surface conditions of the skin, by their effect upon the coefficient of friction between skin and the rubbing agent, control the number of rubs

required to produce a blister. There is an inverse relationship between the frictional force and the number of rubs required to produce a blister.

Reduction of the frictional force between skin and the rubbing agent appears to afford protection to the skin in two ways: first, by lowering the amount of work done on the skin per rub; second, by increasing the total amount of work which the epidermis can withstand. Possible mechanisms of this are discussed.

Blister formation appears to occur in two independent stages; first, prickle-cell necrosis which causes an intra-epidermal split, and second, the filling of this with fluid, probably from the dermis. It is the ease with which an intra-epidermal split is formed which is being measured in these experiments.

The prickle-cell necrosis is unlikely to be due to a local heating effect and there is no evidence that it is enzymically determined; it is not influenced by short-term changes in dermal blood flow or by the intensity of the triple response. It is suggested that the prickle-cell necrosis is caused by repeated cellular distortion which might cause a denaturation of the cellular protein.

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The histological work was done by Dr. I. Whimster of the Department of Pathology, St. Thomas's Hospital Medical School.

The statistical analysis of results was done by Dr. J. M. Tanner of the Department of Physiology, St. Thomas's Hospital Medical School.

I would like to thank Professor E. P. Sharpey-Schafer for the facilities and help of the Department of Medicine, St. Thomas's Hospital Medical School and Dr. D. O'Neill for referring patients to be investigated.

I would also like to thank the following people for help in the preparation of this paper: Miss Joan Dewe for the preparation of the figures, Mr. Morman and his colleagues for the photographic reproduction of the figures, Mr. Clark for the photomicrograph, and Miss Leicester for the typescript.

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SULPHYDRYL GROUPS AND DISULPHIDE LINKAGES IN HUMAN EPIDERMAL COMPONENTS.*

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THIS study deals with the concentrations of sulphydryl (-SH) groups and disulphide (-S-S-) linkages in the cellular and keratinous fractions of human epidermis. The values found were compared with those obtained in homogenates of whole epidermis.

MATERIALS AND METHODS.

Human epidermis was obtained from three sources: (i) Strips of abdominal epidermis from autopsy material. (ii) Samples of skin from surgical specimens, such as amputated legs. (iii) Skin from stillborn infants.

The epidermis was separated from the corium by the stretch method of Van Scott (1952), dried in a vacuum exsiccator or in an incubator at 37° C. and pulverized in a porcelain mortar. For the fractionation of the epidermis, the powder was passed through a 200-mesh sieve and defatted in a glass-stoppered centrifuge tube by washing three times with ether. Before the last ether-washing, the suspended epidermal powder was thoroughly stirred up by inverting the centrifuge tube several times. The powder was then allowed to settle before the final centrifuging.

In the centrifuged powder two layers develop. The upper layer is less pigmented and of chalk-like appearance, the lower layer is darker and granular. These distinctive features are well marked in the Negro epidermis. After the ether-washed powder is dried in the incubator, the two layers can be easily separated. Histochemical identification of the upper layer as the keratinous and the lower as the cellular layer has been described previously (Flesch and Satanove, 1952).

Two methods were used for the preparation of epidermal homogenates. In both methods the skin surface was first thoroughly cleaned with ether. By the first method, after stripping, the epidermis was immediately weighed and homogenized in water (15 mg. wet weight/ml.). An aliquot of the same epidermis was dried to determine its water content. By the second method the

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separated epidermis was dried for 24 hours in an incubator at 37° C., defatted with ether and homogenized with water (5 mg. dry weight/ml.), as described in previous studies (Griesemer and Gould, 1954).

Sulphydryl groups were determined with Bennett's reagent (Flesch and Kun, 1950). The original method was simplified with a stable endpoint by directly measuring the absorption of the dye in the Klett-Summerson colorimeter with filter No. 47, without the addition of concentrated hydrochloric acid. For the estimation of potentially available -SH groups, 10-15 mg. samples of the upper and lower layers of the epidermal powder were incubated with $\frac{1}{2}$ -1 ml. of 10% Duponol (sodium lauryl sulphate) for 1 hour at 40° C. (Van Scott and Flesch, 1954) or at room temperature. Homogenates were incubated with equal volumes of 20% Duponol.

Disulphide linkages were determined in samples containing 4 mg. of tissue, after incubating them for one hour in a boiling water-bath with 1 ml. of 2 M KCN in 0.1 N NaOH (final concentrations). Boiling with KCN reduces the -S-S- linkages to -SH groups, each -S-S- bridge yielding one -SH group which then can be estimated with Bennett's reagent.

All determinations were carried out on duplicate samples; only results agreeing within 10% were accepted.

RESULTS.

Sulphydryl and disulphide values in the layers of sifted human epidermis are represented in Table I. Since the keratinous and cellular components

TABLE I.—*Sulphydryl Groups and Disulphide Linkages in Keratinous and Cellular Components of Human Epidermis.**

Type of epidermis.	Number of specimens.	Cellular layer.			Keratinous layer.		
		-SH	-S-S-	-SH + -S-S-	-SH	-S-S-	-SH + -S-S-
White infant . . .	5 .	64 ± 45	284 ± 30	348 ± 35 .	39 ± 7	330 ± 49	369 ± 45
„ abdomen . . .	7 .	47 ± 11	243 ± 43	290 ± 42 .	30 ± 7	318 ± 48	338 ± 57
„ leg . . .	5 .	49 ± 17	307 ± 21	356 ± 13 .	35 ± 10	374 ± 17	409 ± 31
„ sole . . .	5 .	27 ± 7	269 ± 34	296 ± 38 .	20 ± 5	273 ± 33	293 ± 38
Coloured infant . .	5 .	47 ± 12	318 ± 34	365 ± 38 .	27 ± 9	294 ± 44	321 ± 45
„ abdomen . . .	5 .	43 ± 16	257 ± 19	300 ± 30 .	24 ± 8	304 ± 27	329 ± 32
Average . . .	.	46 ± 13	280 ± 30	326 ± 37 .	29 ± 8	317 ± 36	346 ± 41

* All values expressed as sulphur in mg./100 g. dry weight of tissue.

derive from the same piece of epidermis, in individual determinations each sample of epidermis serves as its own control and from certain consistent differences the following conclusions could be drawn :

(i) In the 32 specimens analyzed, the -SH values represent only a fraction of the "total" (-SH — -S-S-)* sulphur. In the horny layer they amount to

* Methionine determinations were beyond the scope of this study.

8%, in the cellular layer to 14% of the "total". With one exception (one sample of Negro abdominal epidermis) -SH values were about 60% higher in the cellular layer than in the keratinous layer.

(ii) In 28 of the 32 specimens analyzed, -S-S- values on the average were 12% higher in the horny layer than in the cellular layer. Exceptions were found in two samples of plantar epidermis and in epidermal strips of one white and one coloured infant.

Some of these relationships are schematically illustrated in Fig. 1. Theoretically the average "total" (-SH + -S-S-) sulphur should probably be identical in the two layers. The differences found are within the experimental error.

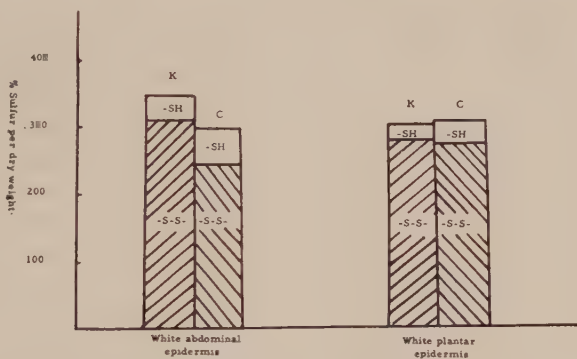


Fig. 1.—Sulphydryl (-SH) groups and disulphide (-S-S-) linkages in keratinous (K) and cellular (C) layers of white abdominal and plantar epidermis.

Storage of the dried epidermal powders at room temperatures for several months did not affect their -SH or their -S-S- content.

In homogenized specimens there was no distinct separation of the epidermis into cellular and keratinous layers. A coarse degree of separation could be achieved in thoroughly pulverized, unsifted specimens. Sulphydryl values in homogenates of whole epidermis were more variable and considerably (two to three times) higher than in the sifted powder. However, the differences in the -SH values of the keratinous and cellular components of pulverized unsifted epidermis still showed the same relationship as was obtained in sifted specimens. Disulphide values were essentially the same in homogenates as in the sifted powder.

DISCUSSION.

The method of pulverization and sifting permits a uniform and fairly complete separation of the epidermis into keratinous and cellular components. In contrast to this, homogenized specimens did not permit such a fractionation. However, the disadvantage of pulverization and sifting, as compared with homogenization, was a marked reduction in the -SH values, probably caused by oxidation of these groups in the process of sifting. In spite of this dis-

advantage, the technique of sifting was used, because it permitted the estimation of -SH and -S-S- in relatively pure epidermal fractions. Since both layers of the epidermis are subjected to the same treatment prior to determinations, one can presume that relative differences in the reported -SH and -S-S- contents between the cellular and keratinous layers of the epidermis retain their validity.

Disulphide bridges can be estimated only after their reduction to -SH groups. For this reason there are certain inherent difficulties in the estimation of these groups in tissues which contain both -SH groups and -S-S- bridges. In such tissues, after reduction with KCN, the estimated -SH values include both the originally present -SH groups and those resulting from the splitting of -S-S- linkages. There is no way of estimating the extent to which boiling KCN affects the originally present -SH groups. In this work we assumed that the -SH values obtained after boiling with a 2 M KCN solution represent both the originally present -SH groups, and those obtained through the reduction of -S-S- linkages. In sifted epidermal powder the amounts of the originally present -SH groups which may be destroyed during boiling are relatively so small that "total" (-SH + -S-S-) sulphur values are only insignificantly influenced by their destruction.

Our previous (Van Scott and Flesch, 1954) and present works indicate that most of the -S-S- linkages in the horny layer originate from those already present in the Malpighian layer, but there is no evidence that they arise from the oxidation of -SH groups. In other words, *a -S-S- containing keratin precursor occurs in the living cellular layers of the epidermis*. This finding is in contrast with the classical concepts of -SH and -S-S- metabolism in epidermal keratinization. These old concepts stated that the metabolically inert horny layer has no free sulphydryl groups; its disulphide bridges were supposed to stem from the oxidation of the sulphydryl groups of the Malpighian layer (Giroud and Leblond, 1951).

The possible nature of the hypothetical keratin precursor in the Malpighian layer has been discussed in a previous publication (Van Scott and Flesch, 1954). Many aspects of this process of "intra-epidermal keratinization" remain to be clarified, and one of the least understood problems is the origin of this intra-epidermal keratin precursor. Recent histochemical evidence indicates that -S-S- linkages occur in the entire Malpighian layer (Barnett, 1954). Our present study also indicates that the process of keratinization begins in the Malpighian layer. Variations in this process may occur, as shown by the differences in the -SH/-S-S- ratios found in different types of skin.

SUMMARY.

1. Sulphydryl (-SH) groups and disulphide (-S-S-) linkages were estimated in the cellular and keratinous components of pulverized and sifted human

epidermis. These values were compared with those obtained in epidermal homogenates.

2. The -SH groups in pulverized and sifted specimens represent only a fraction of the "total" (-SH + -S-S-) sulphur and are present in both epidermal components. The cellular layer contains higher amounts than the keratinous layer.

3. Disulphide concentrations are only slightly higher in the keratinous fraction than in the cellular fraction.

4. These findings support the theory that a -S-S- containing keratin precursor occurs in the living cells of the Malpighian layer. There is no evidence to indicate that the majority of the -S-S- bridges in the horny layer originate from the oxidation of the -SH groups of the Malpighian layer.

We are indebted to Dr. Donald M. Pillsbury for his interest and encouragement and to the Department of Pathology, University of Pennsylvania Hospital, for their co-operation in supplying us with experimental material.

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DISSOCIATED DEPIGMENTATION IN VITILIGO. SIGNIFICANCE AND THERAPEUTIC IMPLICATIONS.*

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It has been pointed out by Billingham and Medawar (1948, 1953) that "the melanocyte system of the skins of man, guinea-pig, pig and cattle consists of two anatomically and (in some degree) physiologically distinct parts; that belonging to the hair bulbs and responsible for the pigmentation of hair and that belonging to the basal layer of the superficial epidermis". They are anatomically distinct because the melanocytes of the basal cell layer of the epidermis stop short at the hair-follicle neck, and then there is a gap until the hair-follicle bulb is reached when another set of melanocytes is found. They are physiologically distinct since in human beings black hairs often emerge from white skin, in pigs white hairs emerge from black spots, and in guinea-pigs red hairs can spring from black skin. Billingham and Medawar point out that these two sets of melanocytes are interchangeable, since if a Thiersch-graft thickness of the hairy skin of a guinea-pig is removed, leaving the bases of the hairs intact, then the raw area will be recovered both by Malpighian cells and by melanocytes from the hair bulbs; further, using cell suspensions black melanocytes can be introduced into red or white hair follicles and can result in the production of black hairs.

Now these observations may throw some light on the problem of vitiligo, since very commonly one sees pigmented hairs growing through vitiliginous patches. This is naturally more obvious in brunettes than in blondes. This dissociated depigmentation can be seen, for example, in the photographs published by Sidi and Bourgeois-Gavardin (1953) in their paper on the treatment of vitiligo with *Ammi Majus Linn.* In vitiligo the depigmented skin possesses melanocytes, but these are of the "white" variety, i.e. they lack the ability to produce pigment. The pigmented hair follicles however possess fully functional "black" melanocytes. If the epidermis from a patch of vitiligo with dark hair is removed, leaving the hair roots intact, regeneration from the hair follicles should result in repigmentation of the patch.

In order to find out whether this would in fact occur, the first step was to remove a Thiersch-graft thickness from an area of vitiligo with pigmented hairs.

* Paper read at the Meeting of the British Association of Dermatology at Cambridge, June 1954.

The skin removed was discarded and the bare area became recovered in the ordinary way in the course of time. This was done on two patients, in one of whom (an Indian) the area began to repigment 21 days after the operation and was densely pigmented 2 months later. The other, a white woman, did not repigment.

A second procedure carried out on the same two patients was to produce epidermal removal by blistering with carbon-dioxide snow. Transient repigmentation resulted in the Indian, none in the white patient. The explanation of this partial failure will be discussed later. The third method was to produce blistering, or at any rate epidermal necrosis, with a Kromayer lamp; this was tried in three cases and in all resulted in repigmentation. By a fourth method, an attempt was made to produce dermo-epidermal separation by means of heat. The amount of heat used was a little excessive and the experiment was complicated by sepsis, but in spite of this there was a temporary appearance of pigment. Finally, blistering by the local application of cantharidin was attempted but was a failure for technical reasons; this will be tried again later.

As far as they go these experiments support the thesis of interchangeability of melanocytes. In all cases where success was achieved, the pigment appeared in spots around the hair follicles and spread to join up from them. These results suggest that it is quite feasible to colonize vitiliginous skin with active melanocytes from pigmented hair follicles.

A word about the blisters produced with carbon-dioxide snow. Why was there a relative failure of repigmentation in the two cases in which it was tried? The most likely explanation that springs to mind is the susceptibility of melanocytes to cold. This has been demonstrated by Taylor (1949). He froze the skin of dark-haired rats with carbon-dioxide snow and with a special cooling device, and found that provided the skin was sufficiently frozen the black hairs of the depigmented area regrew white. This he interpreted to mean that the melanocytes were selectively killed by cold. His experiments suggest however that it might be possible to repigment vitiligo by freezing, if the temperature were critically controlled so as to freeze the basal cell layer without at the same time cooling the hair bulbs sufficiently to destroy the melanocytes.

It may be asked whether the repigmentation produced in these patients is temporary or permanent. It is too early to answer this question. One patient whose repigmentation induced by the Kromayer burn appears to be holding the pigment after 8 months, but another shows signs of fading after 6 months. The repigmentation induced by surgical removal of the epidermis showed signs of fading after 5 months. Are these procedures likely to be of therapeutic value? Once again it is too early to say. They suffer from the drawback that epidermal removal is apt to be unpleasant. The method may however be of value in the treatment of small areas of vitiligo and it is possible that methods of epidermal removal other than those already tried may prove to have advantages, for

example, the sandpaper technique, or chemical removal of the skin using trichloroacetic acid, acid nitrate of mercury, phenol or croton oil. These experiments may also throw light upon the variability of success achieved in the past with ultraviolet radiation, with and without bergamot oil, since success with these methods may be dependent upon the presence of pigmented hairs, and upon the production of blistering or skin necrosis. Finally, the present results may help to explain the mechanism of action of Ammi Majus *Linn.* (xanthotoxin) (El Mofty, 1948 ; Lerner *et al.*, 1953 ; Sidi and Bourgeois-Gavardin, 1953). Plainly if xanthotoxin and light are used in such a way as to produce blistering, the action may be non-specific ; it should be emphasized however that reports suggest that repigmentation can be produced by xanthotoxin without blistering. It is possible that xanthotoxin may cause colonization of the depigmented areas by the melanocytes of the pigmented hair bulbs. This is suggested by reports that repigmentation with Ammi Majus *Linn.* extracts commonly begins in the region of the hair-follicle mouths. If this is so then it may be expected that cases of vitiligo without pigmented hairs will fail to respond to Ammi Majus *Linn.*

SUMMARY.

It has been pointed out by Billingham and Medawar that the melanocyte systems of epidermis and hair follicles are anatomically and physiologically distinct. In vitiliginous skin pigmented hairs are frequently seen. If in such cases the epidermis is removed leaving the hair bulbs intact, regeneration of the epidermis occurs from the latter, resulting in a normally pigmented skin.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. Reginald T. Brain.

16 December 1954.

Darier's Disease.—Dr. F. RAY BETTLEY and Dr. H. HABER.*History.*—A man aged 42.

Served in Regular Army 1935–1945, including service in Egypt, India and Burma, as well as Europe. Had malaria and dysentery in Burma. States he had no skin trouble before his Army Service.

1941 : Developed boils on his back while serving in Iceland. *Condition has persisted since then.*

1944 : Exacerbation of boils while in Burma, treated with penicillin injections. Also developed malaria and dysentery for which treatment given.

1946 : Boils became more troublesome. Treated at Worcester, "sebaceous abscesses" in right scapular and left buttock region incised and curetted; condition diagnosed as "cystic acne vulgaris".

1948 : Treated by a dermatologist with U.V.R., Lotio calaminae with 6% sulphur and vit. A tabs. for four weeks. (Presumably the diagnosis was acne vulgaris.)

1950 : Relapse of amoebic dysentery treated at Southsea Hospital with emetine, iodoquine and quinoxyl.

1951 : First seen at Queen Mary's Hospital, Roehampton and skin biopsies done. At this time, the clinical appearance was very numerous hard plugs contained in follicles on the back of the shoulders and chest, some inflamed suggestive of acne vulgaris. No true comedones.

1953 : Treated at Southampton for clinical amoebic dysentery with a course of terramycin.

November, 1954 : Readmitted to Queen Mary's for tropical check. Blood-count, chest x-ray, E.S.R. normal. W.R. negative. It is now noted that the large follicular plugs have become more numerous and are affecting the limbs.

No treatment has been given.

Diagnosis depends largely on histological features.

Dr. BETTLEY : This patient's eruption began in his early thirties. The easy diagnosis is acne vulgaris, because of its distribution and because it consists of plugged follicles, some of which become inflamed. Three years ago when I saw him first he was in that state. I was struck then by the size of the follicular plugs, and when they were dug out it became evident that they were not plugs of sebaceous material, but were hard cornified masses. I thought that perhaps I was dealing with a diffuse late developing naevus and was inclined to think of it as the condition clearly described by Kyrle as keratosis follicularis et para-follicularis in cutem penetrans, a disorder about which I had always felt dissatisfied in the cases which we have seen in London. I felt dissatisfied with the nosological position of that disorder, and I was dissatisfied also because I thought our cases did not fit in very well with Kyrle's description. The diagnosis of the condition here is entirely due to Dr. Haber, who examined the biopsy sections. I hope you will agree with me that Dr. Haber's exposition of this case in relation to Darier's disease and Kyrle's disease is a very satisfying one and possibly resolves the uncertainty which we may have felt about the latter type of disease.

Dr. HABER : We were fortunate in obtaining several biopsies of different looking lesions from this patient. Clinically there are follicular hyperkeratotic lesions which in some places have

become large enough to simulate at first glance acne conglobata. There is however no tendency to suppurate, and one can remove keratotic lesions with the finger nail, after which more or less deep dimples remain. One can also see a few comedos and a few cyst-like formations. This lesion, however, reveals histologically quite a different picture from the acne group.

Fig. 1 shows a marked hyperkeratosis of four adjacent follicles producing clinically a crater-like lesion. In one place there is a dyskeratotic process in the region of the stratum granulosum followed by a parakeratotic column of cells (Fig. 2). The corium shows only a mild lymphocytic infiltration, and not a subacute granuloma as one would expect in an acne conglobata lesion.

Fig. 3 shows a characteristic lesion of Darier's disease: finger-like processes of rete pegs, clefting and dyskeratosis of the stratum granulosum region, and follicular hyperkeratosis.

On studying these lesions closely one is surprised how some simulate the histological appearance of Kyrle's disease. Fig. 4 exemplifies the histology of a characteristic lesion of Kyrle's disease. In Kyrle's original description the hyperkeratosis was so extreme that it destroyed the stratum spinulosum and penetrated the corium to produce a foreign body reaction. Although many reports of Kyrle's disease have since appeared in the literature, this picture was certainly not met with and one must consider that it is not an absolute postulate for diagnosing this condition. In serial section one can observe in Kyrle's disease a peculiar dyskeratotic process which leads to cleft formation similar to that seen in Darier's disease (Fig. 5). One must not forget that in Darier's disease the presence of corps ronds is not absolutely necessary to diagnose the disease. Cases with verruca plana-like lesions of the dorsa of the hands never show corps ronds but simple clefts as seen in Fig. 5. One can, therefore, assume, without implying that the similar histology suggests a clinical identity, that Darier's disease and Kyrle's disease might be related, or that Kyrle's disease might possibly be a variant of Darier's disease.

Case for Diagnosis. ? Lupus Erythematosus Profundus.—Dr. R. H. MARTEN (for Dr. F. RAY BETTLEY).

Mrs. P. G.—aged 47. Occupation: Housewife.

History.—May 1954: Developed "boils" in the nose. Healing occurred after six weeks' treatment with penicillin and erythromycin.

Early in June 1954: She noticed her nose was swollen, red and blistered.

August 1954: She first attended the out-patient department and at this time showed on the bridge and right side of her nose a dark red slightly raised area 2.5 cm. across. Telangiectases were present on the surface and diascopy revealed a yellowish colour. The area has gradually increased in size to involve the left side of the nose and adjoining part of the left cheek. At times blisters containing serum coloured or yellowish fluid have been observed. These dry up and form crusts, which separate and leave scars. The colour of the lesion has varied between brownish-red and an angry dusky red. The area became sore and more red following exposure to sunlight in August. She complained of shivering and feeling unwell when the lesion was at its height.

Past history.—Four years ago right lacrimal duct obstruction. She has never lived abroad.

Family history.—Nil relevant.

Examination.—There is a dusky-red, slightly raised area involving the sides and bridge of the nose and adjacent portion of the left cheek. Telangiectases are present on the surface and scarring is visible on the bridge of the nose. The left side of the nose is firm and infiltrated and there is considerable soft tissue swelling below the left eye. Liver, spleen, lymph glands—not palpable. Other systems—normal.

Investigations.—(1) Hb 95%. P.C.V. = 44%. W.B.C. = 7000. Polymorphs 67%, lymphocytes 23%, monocytes 9%, eosinophils 1%.

(2) E.S.R. 42 mm./hr.

(3) Blood Wasserman and P.P.R., negative.

(4) X-ray chest and hands, normal.

(5) Mantoux 1:10,000 positive.

(6) Fungus and virus studies, negative.

(7) E.N.T. examination, normal.

(8) Plasma proteins 7.5; albumin 4.5; globulin 3.0%.

(9) L.E. cells—none seen.

(10) Biopsy: Left side of nose. Histology: In the dermis and subcutis there is a

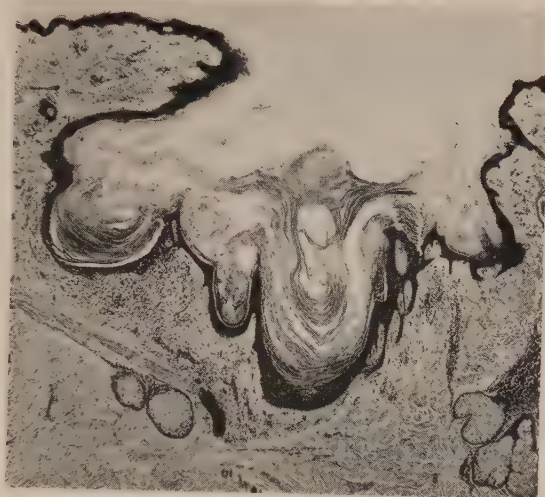


FIG. 1.

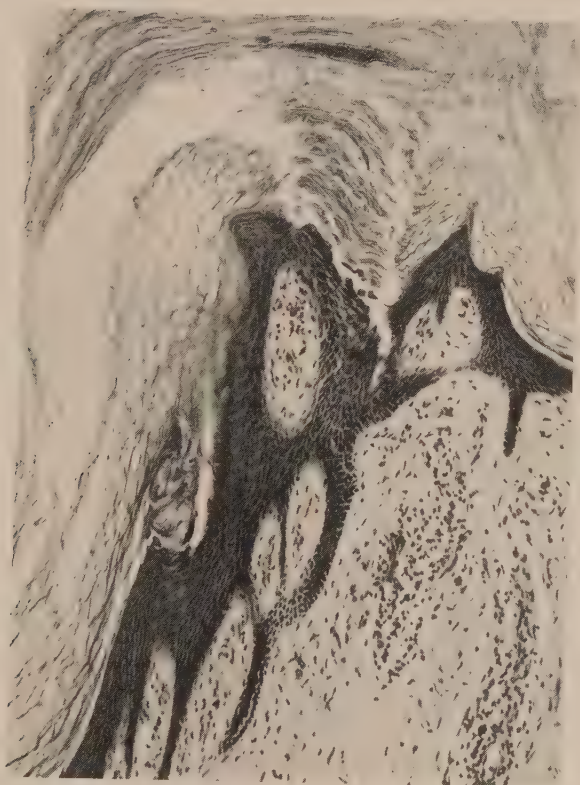


FIG. 2.

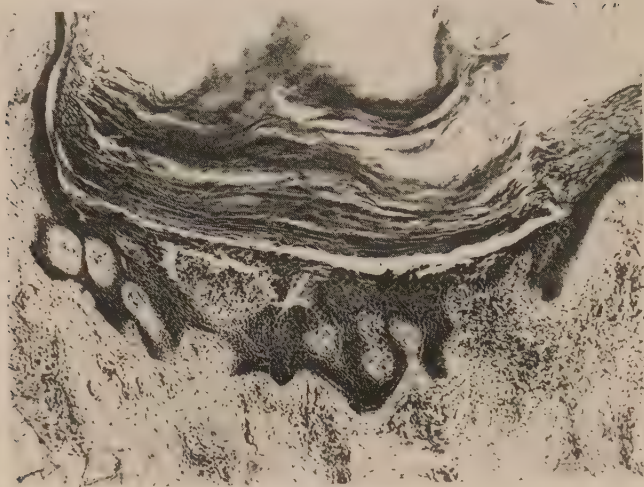


FIG. 3.

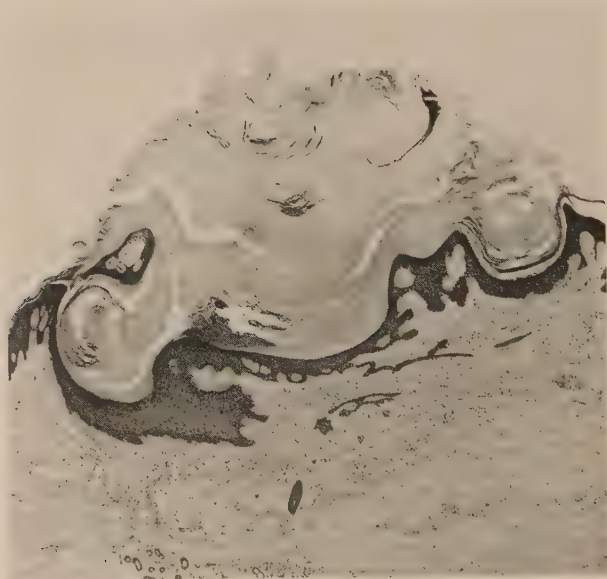


FIG. 4.

dense perivascular and periacinal infiltrate composed mainly of mature lymphocytes with a few reticulum cells. The epidermis is essentially normal.

Treatment.—(1) Isoniazid 100 mg. *t.d.s.* for 2 months with slight initial improvement.

(2) Aureomycin 250 mg. *q.d.s.-t.d.s.* for 5 weeks.

During Aureomycin therapy, the lesion decreased in size and became less inflamed.

When she first attended, the appearances were similar to sarcoid or angiolupoid. However, there was no supporting evidence for the former diagnosis and blistering and crusting are not a feature of angiolupoid. Furthermore, the histology did *not* support either diagnosis.

At various times the lesion has resembled leishmaniasis, but the patient has never lived abroad and no organisms were seen microscopically.

Other diagnoses considered were some form of reticulosis, eosinophilic granuloma, lymphocytoma or an unusual form of lupus erythematosus.

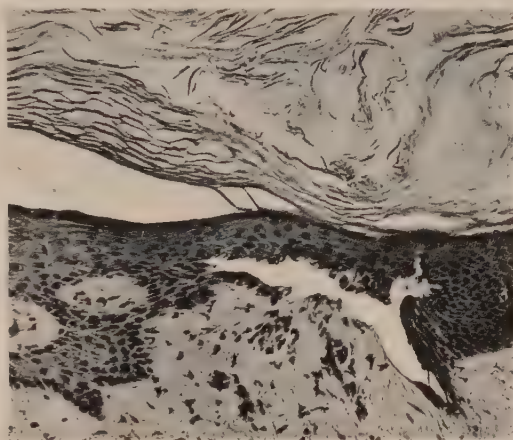


FIG. 5.

The histology with the predominately perivascular lymphocytic infiltrate of mature cells extending down into the fat, might favour the diagnosis of lupus erythematosus profundus rather than a reticulosis.

However, the existence of such an entity has been seriously questioned and some authorities consider that in these cases the deep lesions represent the Darier-Roussy type of sarcoid. Usually in these cases, typical lupus erythematosus lesions are also present. The absence of such lesions, together with the blistering and crusting present in this case, must throw considerable doubt on this diagnosis, and perhaps reticulosis in the right label.

Dr. BRIAN RUSSELL: The patient told me that the exacerbations occur after coryza. There is crust within the left nostril. This may be a recurrent cellulitis from a fissure in the nostril.

Dr. J. S. PEGUM: I wonder whether Dr. Marten's other suggestion of lymphocytoma is not the more probable diagnosis? There was a distinct apple-jelly appearance at the periphery of the lesions. The light sensitivity is consistent with the diagnosis of either lymphocytoma or with lupus erythematosus.

Dr. L. FORMAN: I think the histology favours the diagnosis of lymphocytoma and it may be that blood changes are already occurring, for the blood count was somewhat abnormal. The edema which is present is unusual for lupus erythematosus.

Dr. J. E. M. WIGLEY: I would like to support Dr. Brian Russell's suggestion in asking if any bacteriology has been done. In addition to the possibility of it being infected I think there is quite likely to be an element of innocent artefact.

Dr. I. B. SNEDDON: This case reminds me of one shown to me by my colleague in Sheffield, Mr. Doris Fletcher, in which the diagnosis turned out to be a reticulosarcoma. (This case was shown at an unofficial local meeting in Sheffield in 1953 and was not published.)

Dr. H. HABER : The changes in the epidermis exclude lymphocytoma. The infiltrate occupies the entire corium to reach also the upper parts of the subcutis. The infiltration consists of round cells, but there are also many reticulum cells, some multinucleated. The histology therefore suggests rather a reticulosis than lupus erythematosus.

Postscript.—Early in January 1955 the inside of her nose became blocked by a mass of necrotic crusted material. Histological examination showed a reticulum cell sarcoma. Deep x-ray therapy to a total dose of 5490r in twenty-seven treatments over thirty-three days was completed on the 23 February 1955. When seen about end of March, her nose was of normal size and shape apart from scarring on the bridge, and the airway was clear. Except for a few adhesions the inside of the nose was normal.

The following cases shown have been published in *Proc. roy. Soc. Med.* **48**, 445.

Lichen Planus Pemphigoides.—Dr. B. SCHWARTZ.

Median Lethal Granuloma of the Face, treated with radiotherapy.—Dr. R. G. HOWELL (for Dr. B. G. MITCHELL-HEGGS).

The following cases also were shown.

Pityrias Rubra Pilaris.—Dr. R. H. MARTEN (for Dr. F. RAY BETTLEY).

Angiokeratoma.—Dr. E. N. M. JOHNSTON (for Dr. E. W. PROSSER THOMAS).

An Early Squamous Cell Carcinoma (five weeks) : An early squamous cell Carcinoma (five weeks), clinically simulating molluscum sebaceum : Scleroderma with Auricular Fibrillation.—Dr. E. J. MOYNAHAN.

NORTH BRITISH DERMATOLOGICAL SOCIETY.

Dundee, 9 June 1955.

Case for diagnosis. ? Connective Tissue Naevus.—Dr. O. A. FINN.

R. F—, boy aged 6 years.

History.—At the age of nine months a small raised spot was noticed on the abdominal wall. This lesion gradually increased in size and assumed a yellowish tint. Fresh lesions have appeared at intervals on the trunk, especially on the flanks. No subjective symptoms. General health unimpaired.

Past History and Family History.—Nil relevant.

Present Condition.—About 5 in. above the umbilicus there is a raised well-defined yellowish lesion of 2.5 cm. diameter. On the abdominal wall and on both hips there are groups of small skin-coloured nodules (0.5 cm. $\times$ 1 cm.) which are firmer to touch than the surrounding skin and are more easily appreciated by palpation than by inspection. No evidence of herniation.

Ocular finding: No angioid streaks.

Blood cholesterol—190 mg./100 ml.

Histology.—(From a recent lesion on the back) Serial sections show no abnormality of dermis or epidermis.

(From the original lesion on abdominal wall) Sections were stained for fat and elastic tissue as well as with H. and E. The only appreciable abnormality seen is some coarsening of the collagen bundles. There is no abnormal lipid deposition, no inflammatory reaction and no recognizable abnormality of the elastic tissue of the corium.

Comment.—The condition appears to be similar to that described by Prakken 1952, *Brit. J. Derm.*, **64**, 87) as connective tissue naevus.

The following cases also were shown :

Pemphigus Foliaceus ; Cutaneous Leishmaniasis ; Infantile Eczema (Lipomelanitic Reticulosis) ; Pemphigus Vulgaris.—Dr. J. KINNAR.

Juvenile Dermatitis Herpetiformis ; Pretibial Myxoedema with Ulceration.
—Dr. T. K. BUCHANAN.

Rodent Ulcer Simulating Keratoacanthoma ; Xanthomatosis.—Dr. J. ROGERS.

Multiple Rodent Ulcers. Dr. O. A. FINN.

BRITISH ASSOCIATION OF DERMATOLOGY.

THE Thirty-fifth Annual Meeting of the Association was held in Birmingham on 7, 8 and 9 July under the Presidency of Dr. B. C. Tate. Sixty-nine members attended and there were 22 guests.

The Annual Business Meeting began with the reports of the editor and treasurer which were adopted. Additions and alterations to certain rules were then agreed. It was decided that the next Annual Meeting should be held in London under the Presidency of Dr. G. B. Dowling.

The following officers were then nominated and elected :

President :	Dr. G. B. Dowling
Hon. Treasurer :	Sir Archibald Gray
Hon. Secretary :	Dr. H. J. Wallace
Editor :	Dr. F. Ray Bettley
Assistant Editor :	Dr. G. W. Bamber.

Ordinary Members of Committee :

London :

Dr. Hugh Gordon
Dr. A. D. Porter
Dr. P. D. Samman
Dr. B. C. Tate
Dr. J. E. M. Wigley
Dr. D. I. Williams

Provinces :

Dr. J. H. Twiston Davies
Dr. G. A. Hodgson
Dr. Grant Peterkin
Dr. I. B. Sneddon
Dr. J. Sommerville

Sir Archibald Gray, Dr. G. B. Dowling and Dr. J. E. M. Wigley were elected Trustees of the Association.

The following honorary members were then elected : Dr. Henry Semon and Dr. J. Ferguson Smith.

After this Professor A. Crosti, Professor S. Lapière, and Professor J. R. Prakken were elected honorary foreign members.

The following were elected ordinary members of the Association : Group Captain H. E. Bellringer, Dr. G. Henly, Dr. E. J. Moynahan, Dr. G. W. Senter, Dr. R. H. Seville, Dr. E. J. Waddington.

The Meeting then accepted affiliation of the Queensland Branch and elected as overseas members : Dr. Lorna M. Archibald, Dr. B. B. Barrack, Dr. A. J. Foote, Dr. J. W. Heaslop, Dr. N. Y. McCallum, Dr. O. E. Nothling, Dr. C. Petherbridge.

The main subject for discussion was Industrial Dermatoses. This was opened by Professor J. R. Squire, followed by Dr. G. A. Hodgson, Dr. J. H. Twiston Davies and Dr. J. K. Morgan and finally a paper by Dr. S. R. Wood.

In the afternoon the following papers were read :

Dr. G. C. Wells and Dr. C. D. Calnan : " Sensitivity to Nickel ".

Dr. P. D. Naylor : " Friction blisters in Normal and Abnormal Skin ".

Dr. A. Jarrett : " Fluorescent Microscopy ".

Mr. George Szabo : " The Structure of Human Epidermis and the Numerical Distribution of Melanocytes as demonstrated by the Skin-splitting Technique of Medawar ".

Dr. W. R. Bett : " The Skin of the Mighty ".

The next morning there was a discussion on " Diseases due to Fungi ", which was opened by Dr. R. W. Riddell, followed by papers by Dr. C. D. Calnan, Dr. Cleveland White, Dr. J. G. Holmes, Dr. C. H. Whittle and Dr. A. J. Rook. Dr. J. S. Pegum read a paper on " The Therapeutic and Toxic Effects of Large Doses of Vitamin A ".

The afternoon was spent in various ways : visits to several factories were arranged, while others competed for the Golf Trophy.

For Saturday morning, the 9th, there was arranged a demonstration of clinical cases, in which twenty-nine most interesting patients were shown and afterwards discussed.

Throughout the period of the meeting we enjoyed excellent weather and were able to see Birmingham and the surrounding country at its best. On Thursday evening we were invited by Dr. and Mrs. Tate to dine, whence we proceeded to the Shakespeare Memorial Theatre to a charming performance of *Twelfth Night*. This delightful evening will be remembered for a long time.

The Annual Dinner took place at the Grand Hotel, Birmingham, on Friday evening. The principal speakers were Dr. Grant Peterkin, who proposed the health of the guests and Dr. A. P. Thomson, Dean of Birmingham Medical School who replied : Dr. F. R. Bettley who proposed the health of the President and of the Association and Dr. B. C. Tate who replied. The Golf Trophy was presented to Dr. R. Hall, who had won the cup during that afternoon.

By common consent it was agreed that this Birmingham meeting was well up to standard and will long be remembered for the excellence of the papers presented, for the interest of the cases demonstrated, and no less for the charming and generous hospitality of Dr. and Mrs. Tate and their colleagues.

THE NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY.

It is announced that the Ninth International Congress of Dermatology will be held in Stockholm under the Presidency of Professor Sven Hellerström from 31 July to 5 August, 1957. Details may be obtained from the Secretary-General, Dr. Flodén, Hudkliniken, Karolinska sjukhuset, Stockholm 60, Sweden.

BOOK REVIEWS.

MODERN TRENDS IN BLOOD DISEASES.*

IN this book there are fifteen chapters on various aspects of haematology. Each is really a monograph on the present position in the particular subject concerned by an internationally known authority—many from the United States.

Thus, Mr. D. Ll. Griffiths writes on bone changes and blood diseases, Dr. M. C. G. Israels on haematological techniques and the reticuloses (one chapter on each), Dr. Wilfred Gaisford on paediatric haematology, Professor Carl Moore and Dr. R. Dubach on iron metabolism using radio-iron, Dr. C. Rimington on blood pigments and porphyrins, Col. W. H. Crosby and Professor William Dameshek on haemolytic anaemia, Professor M. M. Wintrobe and Dr. E. Cartwright on iron, copper and porphyrin metabolism in the anaemia of infection, Mr. Dennis B. H. Dawson on changes in the fundus in diseases of the blood, Dr. J. F. Wilkinson, B. J. Leonard and C. Gardikas on the acute and chronic leukaemias (one chapter each), Dr. Alexander Brown on anti-coagulant therapy, Dr. C. C. Ungley on Vitamin B₁₂ and the megaloblastic anaemias, Dr. F. Stratton on iso-immunisation to blood groups antigens and Dr. J. H. Twiston Davies on the dermatological aspects of blood diseases. The cutaneous manifestations of many blood diseases—for example leukaemia, reticuloses—have been known for many years, but Dr. Twiston Davies classifies them and gives some idea of their frequency of occurrence.

All the articles are well written, informative, readable, interesting and up-to-date accounts of the subjects in which rapid advance has been made in the last few years. The book has been superbly produced, the paper, printing and reproduction of illustrations all being of the highest class.

The book is a mine of information which can be unhesitatingly recommended to all physicians.

J. K. S.

ROXBURGH.†

THE pleasure which in the past has attended the reviewing of successive editions of "Roxburgh" is dimmed by the knowledge that its distinguished author has now corrected its proofs for the last time, though it is not to be doubted that so eminently useful and practical a book will live on into many more editions.

As in the past changes are relatively few but most recent advances find mention. New antibiotics continue to appear and hydrocortisone ointment is now available in this country, as it was not when the text was written. Sulphonamides are rightly condemned in the treatment of acute lupus erythematosus, but they are considered permissible in that of the chronic form, which is rather against the present consensus. Modern views on the bullous dermatoses are well set out, and the caution (p. 470) against too implicit an acceptance of histological and cytological criteria seems to-day

* *Modern Trends in Blood Diseases*. Edited by J. F. Wilkinson. (1955). London: Butterworth & Co. Pp. 359. Figs. 92. Price 65s.

† *Common Skin Diseases*. By A. C. ROXBURGH. 10th Edition. (1955) London: H. K. Lewis & Co. Ltd. Pp. 516. Figs. 215 and 8 coloured plates. Price £1 10s.

almost prophetic. Chloroquine for actinic dermatitis deserves mention, as do several of the newer antibiotics in the pyodermias. Keratoacanthoma has a paragraph to itself, which is proper as it is by no means a rarity, but it might well have been included in the differential diagnosis of squamous epithelioma. The statement that radiotherapy is contra-indicated in malignant melanoma is too sweeping.

This tenth edition fully lives up to the high reputation established by its fore-runners, and in its avowed sphere of general practice can unreservedly be recommended.

J. F. S.

MODERN COSMETICOLOGY.*

THE first edition of this book appeared in 1940 and contained 288 pages. Through successive editions it has progressively increased in size and now contains nearly 800 pages. This considerable increase in volume presumably results partly from the fact that the author is endeavouring to satisfy the needs of more than one type of reader. Over 100 pages are devoted to the anatomy and physiology of the skin and allied subjects; sections deal with the penetration of the skin by external applications, allergy and dermatitis, and even acne. This part of the book is presumably intended for practising beauticians. It is not impossible to find fault with occasional statements which are made, but on the whole these parts of the book are carefully written and contain a good deal of accurate information. The author has read widely in dermatological literature.

Other sections of the book contain considerable detail of the manufacture of cosmetics: 40 pages are devoted to emulsions and further sections to practical considerations in the manufacture of cosmetics. These parts of the book appear to be mainly intended for manufacturers.

The dermatologist will be principally interested in the information which this book gives concerning the ingredients of cosmetic products. There is not a great deal of this book which the medical man would wish to read systematically, but the practising dermatologist will find here a great deal of information to which he may refer in the course of clinical work. The section on sunburn and light screening is of particular interest.

There remains in this book a certain amount of material, the value of which is doubtful. The chapter on "The Tooth and Pathological Dental Conditions" seems out of place in this volume, but presumably its inclusion merely indicates how wide is the field of Cosmetology in these days.

F. R. B

THE 1954/1955 YEAR BOOK.†

THE *Year Book* reappears year by year like a handsome, hardy perennial. As with a flower, its annual bloom excites admiration, but apart from favourable comment, there is little to be said that has not been said before. This year the authors' own chapter is devoted to recent advances in dermatological mycology. This excellent section calls for no special comment and it is interesting to see that in U.S.A. dermatologists are reaching conclusions similar to those in the United Kingdom—that in fungus infection the part played by host-susceptibility is of very great, and possibly greater, importance than the characteristics of the micro-organisms. It is rather noticeable that in this section 37 references are given to the literature; of these no

* *Modern Cosmetology*. By R. G. HARRY. Fourth Edition. (1955) London: Leonard Hill (Books) Ltd. Pp. 786. Figs. 119. Price 65s.

† *Year Book of Dermatology and Syphilology* 1954 1955. By M. B. SULZBERGER and R. L. BAER. (1955) Chicago: The Year Book Publishers Inc. Pp. 472. Figs. 56. Price 45s.

less than 31 are from the American literature and not one originated from Great Britain. It is to be hoped that this does not represent the real proportion in which British dermatology contributes to the subject.

The remainder of the book takes the usual pattern and is well up to the standard which makes it of very great value to all dermatologists. F. R. B.

PSYCHOCUTANEOUS MEDICINE.*

LET it be said at once that this is a book well worth study by every dermatologist. It is a review of writing and thought on the subject, well up to date, and backed by a bibliography extending to over 40 pages in which this country contributes at least its due share. The author, from his fund of experience, contributes his verdict on the various views he discusses.

That the psyche can influence the skin is a fact which man has realized from time immemorial. It has long become a thing of common speech, and the usual misquotation of "by the skin of one's teeth", which Dr. Richard B. Evans makes in his excellent chapter on "Dynamic Consideration of the Psyche" is an instance not only of the universality of the conception but of its antiquity, for it comes from the Book of Job, some 3000 years old. A refreshing characteristic of this book is that, while it deals frankly with the subject, including its Freudian implications, there is nothing in it which will bring the blush of shame to the cheek of the most thin skinned reader. (How naturally one uses the psychocutaneous idiom!)

Notwithstanding the antiquity of the concept the serious study of psychocutaneous medicine is, as the author points out, of recent date. It is in its infancy and one cannot expect to find here or anywhere else the complete answer to the problem. The author's views are full of common sense: the benefits and limitations of psychiatry, the responsibility of the dermatologist, not only for being, as every doctor has to be, a psychologist, but for knowing his subject thoroughly and avoiding both the Scylla of the indignant zoologist, to whom it was suggested he was suffering from delusions when in fact he had an infestation by a rare mite, and the Charybdis of considering every seasonal dermatitis due to contact when "the flowers that bloom in the spring . . . have nothing to do with the case". Perhaps this balanced aspect of the author's outlook is most prominently displayed in his careful and sympathetic consideration of religious stigmata.

There is no agreement as to which dermatoses can be included under the title of this book. The author considers many classifications and follows his own. Here is an excellent basis from which each of us can try to clarify his own ideas, and the chapter on theories and methods of study is a stimulation to work them out.

If a non-psychiatrically trained dermatologist can criticize such a work he may be permitted to wonder why "sexual" factors are so stressed and "sensual" omitted. The castrated cat is just as responsive to tickling the back of the neck as is the most virile tom. Is every pleasurable stimulation of the skin a "sexual" one? Again, the dermatologist can easily find a psychic factor in 100% of his patients, but in many this is the consequence of the disease and nothing to do with the cause or the course. A patient may accept an internal disease without mental trauma, but any blemish on the skin can cause at least some mental perturbation: and the dermatologist, while treating "the patient" in any case, has to separate those in whom the psyche is influencing the disease from those in whom the disease has upset the psyche; where is the dividing line between the two?

Finally, aided by excellent printing, and in spite of occasional Americanisms and American spelling, this book is eminently readable. It is a pity that, on the whole, the illustrations are not up to the standard of the text. J. K.

* *Psychocutaneous Medicine*. By MAXIMILIAN E. OBERMAYER. (1955) Oxford: Blackwell. Pp. 487. Many illustrations. Demy 8vo. Price £3 10s. net.

A GERMAN ATLAS.*

THE second edition of this work covers comprehensively in excellent manner clinical pictures seen in both dermatology and venereal diseases, the dermatological part of the Atlas occupying 233 pages, and the venereal diseases the remainder. In the skin section the illustrations comprise 308 coloured plates, 67 monochromes and 15 dermatograms or what is roughly the finger-print response of the skin in some diseases. In the venereal diseases part there are 84 coloured plates and 5 monochromes. The colour of the coloured illustrations is on the whole excellent and little criticism can be offered in this connection.

If any criticism can be offered it might be that in connection with a few plates, for example, Abb. 19 (purpura dysproteinaemica), Abb. 241 (melkerknoten) and Abb. 275 (morbus Hodgkin-Sternberg), the appearances presented could scarcely be called classical; on the other hand, Abb. 284 (traumatic lymphocytoma) is an excellent example.

The plates and typescript are printed on very good paper and the book is beautifully bound.

The annotations are on the whole short and to the point, and only a few errors have been noted. Some minor criticisms may be offered with regard to the treatment mentioned. In general it would be better if the proprietary names for certain drugs were left out and the internationally accepted alternatives given instead. It is surprising that in connection with pityriasis rubra no mention is made of high potency vitamin A therapy; and that tannic acid is still accepted as a treatment for burns.

As would be expected in a textbook by continental authors, the section on venereal diseases is most fully illustrated and annotated. All the pictures here are excellent and the pictures of primary sores on the inner side of an eyelid and on the upper gum are examples of unusual location of the primary infection. The example of the corymbose syphilide is really good; the monochrome of syphilitic leucoderma is also good. The varying appearances of gumma before and after break-down are well illustrated, as are also the clinical appearances in congenital syphilis.

On the whole this is an atlas which should be of use to practitioners and specialists alike and should prove a good reference book, as not only are the familiar pictures illustrated but also many variants that are not so common.

J. S.

GERMAN DERMATOLOGISTS.†

THIS is a medical directory, a "who's who" of all dermatologists "of German language" who were trained at German hospitals and are now practising, both in hospitals and privately. The names include doctors of West and East Germany, Austria and those now living in lost territories. It is interesting to find names of many dermatologists who were compelled to leave Germany and have settled in different countries. They are still regarded as dermatologists "of German language" and are included in this directory.

An appendix contains a list of all German university clinics and their chiefs, the names of all German towns with practising dermatologists, and a list of towns with general hospitals with facilities for treatment of skin diseases. Advisory centres for V.D., cancer and tuberculosis throughout West and East Germany are listed in this useful directory.

H. H.

* *Atlas der Haut-Und Geschlechtskrankheiten.* By WALTER FRIEBOES and WALTHER SCHÖNFELD. 2nd Edition. (1955) Stuttgart: Georg Thieme Verlag. Pp. 292. Illus. 479. Price Dm. 118 (approximately £10).

† *Die Dermatologen deutscher Sprache.* By H. LOEHE and E. LANGER. Berliner Medizinische Verlagsanstalt GMBH, West Berlin, 1955. Pp. 391.

CURRENT LITERATURE

SLEEP CURE OF ITCHING DERMATOSES. P. LAUGIER. (1955) *Ann. Derm. Syph., Paris*, 82, 51.

The author discusses the theoretical aspect and practical details of this treatment and emphasizes the need for complete isolation and a trained staff. He reports three personal cases which benefited and refers to others recorded in the literature. F. F. H.

A CASE OF LUPUS ERYTHEMATOSUS PROFUNDUS. RAMOS E. SILVA and H. PORTUGAL. (1955) *Ann. Derm. Syph., Paris*, 82, 34.

A woman aged 22 presented an erythematous rash over the nose and cheeks together with nodular lesions on the face, arms and thighs. Microscopically the superficial lesions were consistent with lupus erythematosus and the deeper hypodermal ones showed all the features described in lupus erythematosus profundus. The patient was febrile at times and ultimately lupus erythematosus cells were identified. F. F. H.

THE KVEIM TEST IN SARCOIDOSIS. D. G. JAMES and A. D. THOMSON. (1955) *Quart. J. Med.*, n.s., 24, 49.

The Kveim test is the intradermal injection of a heat-sterilized saline suspension of sarcoid tissue. In patients with active sarcoidosis a dusky red nodule develops insidiously at the injection site during the ensuing weeks. Histologically there is characteristic sarcoid tissue. Patients with sarcoidosis may react in similar fashion to injections of B.C.G. vaccine, viable and killed tubercle bacilli, gland tissue of lymphatic leukaemia and even normal splenic tissue. Occasionally simple traumatic lesions may heal with the production of sarcoid tissue in the scar. These antigens produce sarcoid tissue only in patients with sarcoidosis and the phenomenon does not detract from the diagnostic value of the Kveim test. Sarcoid tissue is preferred as antigen because it produces positive results in sarcoid patients more consistently than other substances.

The test was positive in this series in 12 out of 16 cases of sarcoidosis, negative in 28 patients with tuberculosis and in 19 patients with other diseases.

The Kveim test is a simple, safe and specific out-patient technique for providing histological proof of sarcoidosis, an index of activity, an index of the progress of disease and by serial biopsy, a method of evaluating various treatments (in this investigation—cortisone, streptomycin and isoniazid). J. M. B.

OUR PRESENT UNDERSTANDING OF THE CANCER CELL. A. HADDOW. (1955) *Practitioner*, 249, 174.

There is evidence that carcinogens induce malignant change by the gradual deletion of key proteins essential for normal growth, so liberating more primitive synthetic reactions upon which the process of cell division depends. This chemical dedifferentiation parallels the biological dedifferentiation of the cancer cell. Should this conception be substantiated it may offer a prospect of restoration of growth control by substitutive chemotherapy. One group of carcinogenic agents possesses special reactive properties resulting in cross linkage, possibly between the contiguous linear macromolecules of the chromosome itself. Nitrogen mustard possesses this property and research is being conducted with other cross linking agents.

R. J. C.

NONBACTERIAL REGIONAL LYMPHADENITIS (CAT-SCRATCH FEVER). AN EVALUATION OF THE DIAGNOSTIC INTRADERMAL TEST. J. J. MCGOVERN, L. J. KUNZ and F. M. BLODGETT. (1955) *New Engl. J. Med.*, 252, 166.

One hundred and twenty persons were inoculated intracutaneously with antigen derived from infected lymph nodes. The test was positive in 10% of those who had never suffered from the disease. A positive reaction is therefore of little diagnostic value unless accompanied by characteristic signs and symptoms. A. D. P.

AN UNUSUAL EPIDEMIC OF KAPOSI'S VARICELLIFORM ERUPTION. R. T. BRAIN. (1954) *Austral. J. Derm.*, 2, 109.

Six cases appeared in a childrens' hospital. The cause was the virus of herpes simplex, and its source was a child of three who was suffering from his second attack of the disease. Three nurses developed herpetiform lesions on the forearms.

R. E. B.

DIAGNOSIS, PHYSIOPATHOLOGY AND TREATMENT OF ACNE VULGARIS. R. ARON-BRUNETIERE. (1954) *Austral. J. Derm.*, 2, 114.

In this article the author develops the theory of the hormonal basis of acne, attempting to correlate the different varieties of the disease with the results of hormone assays. The latter include vaginal smears, urinary 17-ketosteroid, pregnandiol, folliculin, gonadotrophin and thyrostimulin levels; and the basal metabolic rate.

Treatment varies according to the clinical type of the disease, and may include the usual local remedies as well as injections or implantations of serum gonadotrophic hormone; chloramphenicol or aureomycin are given in selected cases, usually of the recurrent folliculitis and acne rosacea types. Good results are claimed.

[Comment: It is very difficult to assess this paper, but in any such work one would like to see certain data clearly set forth.

(a) Theoretical basis: The issue is greatly complicated by the large number of hormones concerned, and by the admitted unreliability of many of the laboratory methods involved. To deduce a relationship between certain hormonal patterns (e.g. altered androgen/oestrogen ratio) and acne one would need repeated assays on the same patient, demonstrating that the patterns alter significantly during the period of improvement or cure; and that such alterations are bolster up from those observed in strictly comparable control groups. It is no longer sufficient to bolster up confusing data with references to the cosmetic effects of castration or adrenal tumours.

(b) The therapeutic test: In the absence of a sound theoretical basis, the results of treatment must be assessed even more critically than usual. In acne especially, where the possibility of spontaneous cure is always present, no form of treatment can be accepted as of value unless it is established by a statistical study of large numbers of patients treated in comparison with a large control group of the same age and sex distribution, and with acne of the same type and severity.

It is to be hoped that Dr. Brunetiere will be able, from his great experience of such cases, to fulfill these criteria in some future publication.]

R. E. B.

INCONTINENTIA PIGMENTI. EWAN MURRAY-WILL. (1954) *Austral. J. Derm.*, 2, 140.

Report of a typical case, with clinical and histological photographs.

R. E. B.

KERATOACANTHOMA. A. G. FINLAY. (1954) *Austral. J. Derm.*, 2, 144.

A useful summary of clinical and histological features and treatment.

R. E. B.

SKIN MALIGNANCIES. W. GILFILLAN. (1954) *Austral. J. Derm.*, 2, 160.

A very interesting case, most probably of multiple self-healing epitheliomata, demonstrated at a clinical meeting. A male aged 59 gave a typical history. Other members of his family were similarly affected. One generation ago his family lived within 40 miles of Glasgow and it is difficult to avoid the conclusion that they were related to Dr. Ferguson Smith's patients.

R. E. B.

EVALUATION OF THERAPY IN CREEPING ERUPTION. L. J. A. LOWENTHAL. (1954) *Austral. J. Derm.*, 2, 171

Creeping eruption is caused by the larva of *Ancylostoma braziliense*. In the cat or dog, which are its normal hosts, the larva penetrates to the bowel: in the human it dies after wandering about the skin for a time, varying from a few weeks to a year or thereabouts. It is impossible to forecast the length of life of an individual larva, and the results of treatment are correspondingly difficult to assess in a small series of cases. It is, however, possible to work out the expected survival-rate in a fairly large population of larvae, and to compare this rate with the results obtained by treating a large number of patients. Using this method, the author could not satisfy himself that treatment with a number of agents had any effect on the prognosis. He reports on 40 patients, harbouring 96 larvae; and also derives support for his argument from the published series of other workers.

R. E. B.

THE MALIGNANT TUMOURS OF THE SKIN. J. C. BELISARIO. (1954) *Austral. J. Derm.*, **2**, 179.

This is a long article with numerous references but little new material. The substitution of the word *actinodermatitis* for *radiodermatitis* must be deplored; there may be rare occasions when terminological obscurity is necessary within the patient's hearing, but an extension of this habit to the literature can lead to nothing but confusion. Future generations will not have time to sift the desert sands for dermatological Rosetta-stones.

R. E. B.

TOPICAL CORTISONE IN SYPHILITIC INTERSTITIAL KERATITIS. GORDON O. HORNE.(1955) *Brit. J. vener. Dis.*, **31**, 9.

This is a detailed report of 23 patients who were treated with topical cortisone and kept under observation for periods ranging from 6 to 39 months, and the author concludes that topical cortisone is imperative in the treatment of syphilitic interstitial keratitis.

W. G. A.

TREATMENT-RESISTANT SYPHILIS. SHORT REVIEW AND REPORT OF A CASE. R. V. RAJAM and P. N. RANGIAH. (1955) *Brit. J. vener. Dis.*, **31**, 25.

A case of unusually prolonged treatment-resistant syphilis with recurrences is reported. An inveterate allergic sensitivity in the tissues of the host appears to have been induced by inadequate treatment of the original infection. After 3 years of resistance to prolonged therapy with mapharsen and bismuth the lesions responded dramatically to the initial course of penicillin only to relapse at varying intervals from 4 months to 5 years. The fresh lesions healed with arseno-bismuth combination and penicillin, but one can only conjecture as to whether the patient will remain free from further trouble. The treatment-resistant lesions were cutaneous and skeletal.

W. G. A.

YAWS IN MANCHESTER. SYDNEY M. LAIRD. (1955) *Brit. J. vener. Dis.*, **31**, 30.

A study of 48 patients made it most probable that 26 were examples of late yaws. The author discusses the difficulties of diagnosis and suggests that when interpreting positive serological tests in coloured immigrants yaws should be considered in the differential diagnosis.

W. G. A.

DERMATITIS OF THE FEET DUE TO SHOES. HARRY SHATEN and MILTON REISCH. (1954) *Arch. Derm. Syph., Chicago*, **69**, 651.

The authors have studied 49 patients suffering from contact dermatitis of the feet caused by footwear. They found that the majority of cases were due to thermoplastic material in the box toe of the shoes. This material contains various varieties of rubber and resins and the anti-oxidants and accelerators in rubber are considered the basic sensitizers. A detailed description of the various materials used in normal shoe manufacture is given. In some cases dermatophytosis was present in addition to contact dermatitis.

J. K.

ACNE COMEDO IN CHILDREN DUE TO PARAFFIN OIL APPLIED TO THE HEAD. CHAIM BERLIN. (1954) *Arch. Derm. Syph., Chicago*, **69**, 683.

An "epidemic" in a collective agricultural settlement affecting 16 boys and 10 girls aged 2 to 10 years is described. It was found to be due to impurities (unspecified) in the oil used.

J. K.

LOW VOLTAGE X-RAY THERAPY IN DISEASES OF THE SKIN. DONALD M. PILLSBURY, HARVEY BLANK and DONALD J. MADDEN. (1954) *Arch. Derm. Syph., Chicago*, **70**, 16.

The authors treated 550 patients over a period of 6 years with very soft x-rays (H.V.L. Al 0.025 to 0.034 mm.). Individual doses varied from 75 to 500r and total dose up to 6000r. They stress the difficulties of maintaining a steady output and the dangers of variations in the primary voltage. Their results show that the only condition treated in which a regular good effect was produced was superficial epithelioma. Results in various types of dermatitis and eczema, anal and vulval pruritus and in psoriasis showed occasional transitory improvement. The treatment of naevus flammeus by this method was disappointing.

J. K.